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DR. A. S. WARTHIN.

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DEPARTMENT OF REVIEWS

The Journal will make an especial feature of the review of monographs and books bearing upon the field of Internal Medicine. Authors and publishers wishing to subject such material for the purposes of review should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all matter sent will be made in the department of reviews.

Editor

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Observations on the Action of Atropin and Calcium and Parathyroid Preparations in Arterial Hypertension*

By Hugo O. Altnow, M.D., *Minneapolis* and James P. O'Hare, M.D., *Boston*

A REVIEW of the titles of articles published within the last five years on the treatment of hypertension suggests the use of twenty-eight inorganic and organic compounds and glandular extracts. If the articles themselves were reviewed, this number would no doubt be doubled and possibly trebled. This condition of affairs carries with it the inference that none of the various preparations suggested has been quite satisfactory.

Our communication deals with three substances: atropin and calcium chloride used in combination, and parathyroid preparations. Before proceeding further, it will not be out of place to state why our selection fell upon these substances, from the large list at our disposal.

We were first stimulated by a communication by Kylin, (1) who reported four cases of hypertension in which a normal blood pressure was obtained after oral administration of atropin and calcium chloride. This report probably would have attracted no more than passing notice if the use of the drug had been on an entirely empirical basis. Closer examination of the report, however, as well as of other work by the same author, indicated that certain experiments of his and of other investigators to whom he referred, put his work on a suggestive physiological basis. In brief, his conception (1 and 2) is that hypertension is a manifestation of a general nervous disorder and particularly of disordered function or unbalance of the vegetative nervous system. He cites as evidence the variety of symptoms of nervous origin and vaso-motor instability that hypertensive patients complain of: exhaustion, restlessness, insomnia, dizziness, buzzing in the ears, chest oppression, palpitation, tendency to asthma, and others. As further evidence of vaso-motor instability there are the labile blood pressure level and the abnormal or reverse adrenalin reaction (there is a primary drop in blood pressure following intramuscular or intravenous injection of adrenalin). He lays stress on the latter, and according to his interpretation of this phenomenon, it indicates that the parasympa-

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*This study was aided by a grant from the Proctor Fund of the Harvard Medical School for the Study of Chronic Diseases.

thetic or vagus system has mastery over the sympathetic.

According to his views, the same disordered state that is responsible for hypertension may at other times be the underlying causative factor in asthma, migraine or urticaria.

It must be admitted that his theory of the mechanism of hypertension is difficult for us to follow. His theoretical basis for the use of atropin and calcium in hypertension is stated as follows. (1) Reversed adrenalin reaction shows that the para-sympathetic system has mastery over the sympathetic system and atropin paralyzes the vagus. The aim in giving atropin is to aid in restoring the balance between the para-sympathetic and sympathetic nervous systems. (2) Through the work of Kraus and Zondek it has been demonstrated that calcium ion reduces sympathetic irritability. (3) Investigations of Jensen (3) have demonstrated that calcium content of serum is lowered in hypertension.

The normal fasting serum calcium content, determined by the Kramer-Tisdale method in fifty normal subjects studied by Matz (4) was found to vary between 9 and 12 mg., with an average of 10.28 mg. His normals were adults of all ages and there is no constant relation between lowered serum calcium content and increasing age. Kylin, (1) by using the Ward method, found that in subjects under forty years of age, the minimal and maximal values were .15 mg. and .5 mg. higher than in subjects over forty years of age. Grove and Vines (5) give 10.5 mg., and Sherrill and Copp (6) 9.4 to 10.4 mg., as normal figures. The latter also state that of all the constituents of the blood, calcium is one of the most constant. Averaging the values quoted, the usual normal serum figure may be arbitrarily set at 10 to 10.5 mg.

We determined the serum calcium by Collip's modification of the Kramer-Tisdale method in fifteen normal adults of all ages, and twelve hypertension cases. Figure I. The normal values were from 9.6 to 11.4 mg., while in hypertension patients, they were 8.6 to 10.6 mg. On seven hypertension patients, the value was 10 mg. or lower. From the curve, it will be noted that the hypertension cases averaged about 1 mg. lower than the normal subjects.

We treated eleven cases of hypertension in the medical wards and the Out-Door Clinic according to the method advocated by Kylin. They all received calcium chloride 1 G. and atropin .00025 G. four times a day for three to four weeks. In six of these cases it had no effect on the blood pressure. In five other cases it might be credited with having some slight effect. We are reproducing two representative curves, Figure II showing no apparent effect following the treatment, and Figure III showing some reduction in blood pressure. In the latter instance we are reproducing one of the best of the five curves. It must be admitted, however, that in some instances the curves obtained from control cases who received no treatment show as good reduction. Figure IV is an example of a control curve of a nervous woman who was under medical observation, during which time she underwent a cystoscopy. In two other cases treated with calcium alone, it appeared to be without effect.

In connection with the administration of calcium, the objection might be raised that an inadequate amount was given. In this connection we cite the work of Matz, (4) who found that 1.3 G. calcium chloride daily produced an average elevation of 2 mg. after it was administered for eleven days.

with nitrogen retention without hypertension, the guanidin secretion by the kidneys is normal. Major and Stephenson (8) also found that dimethylguanidin had the most marked pressor effect. By injecting calcium chloride alone or in combination with potassium chloride, the pressor effect could be

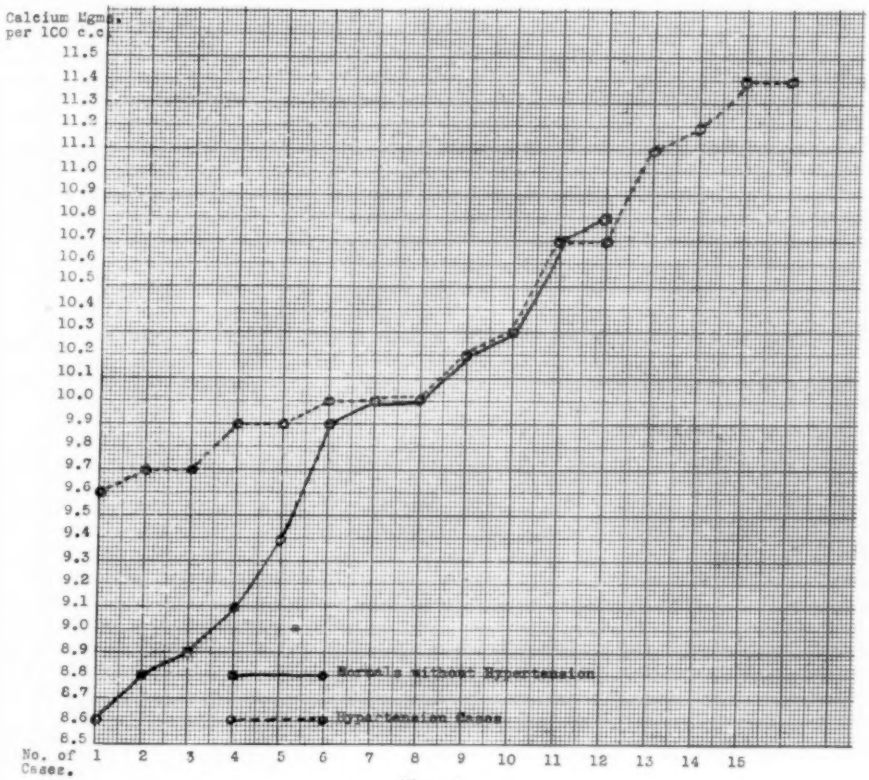


FIG. 1

During the time that we were using the atropin and calcium, Major and Stephenson (7 and 8) demonstrated the prolonged pressor effect of methylguanidin when injected intravenously in dogs. Major (9) also states that guanidin retention occurs on the part of the kidneys in patients with hypertension and chronic nephritis with hypertension, but with chronic nephritis

neutralized, or if injected before methylguanidin, the pressor effect of this substance could be abolished. They conclude that these results suggest that calcium chloride and potassium chloride exert a definite effect on dimethylguanidin.

This work incited in us an interest in methylguanidin, and in our review of the literature, it came to our

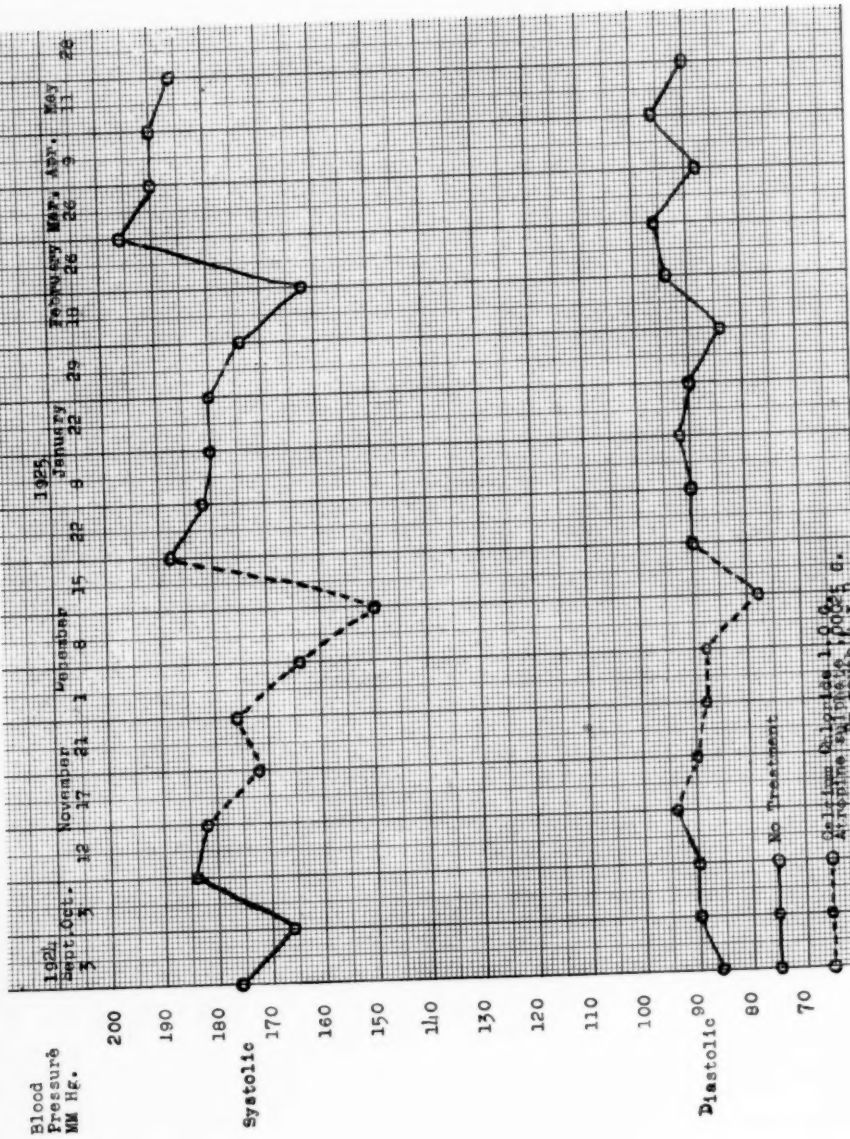

Blood Pressure MM Hg.
Systolic
Diastolic
1924
Sept. Oct. November
1925
January February Mar. Apr. May
No Treatment
Calcium Chloride 1.0 Gr.
Atropine Sulphate 1/200 Gr.
by mouth t.i.d.

FIG. 2

notice that Paton (10) had made some observations suggesting that tetany thyreopriva might be due to intoxication by guanidin bases. Further, Vines, (11) who has done some research on the parathyroid gland, assigns a dual

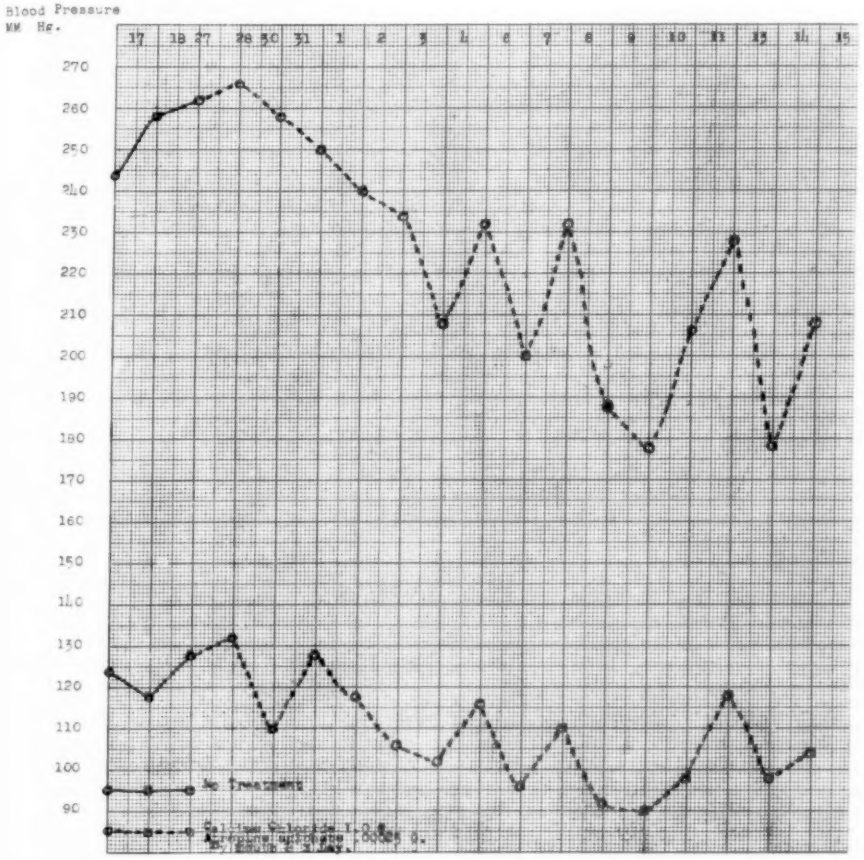


FIG. 3

function to this gland: (1) the removal of certain toxic substances, either guanidin or its methyl compounds, from the blood, and (2) regulation of the calcium metabolism. In a personal communication to Hanson (12) he expressed the opinion that the former action was probably due to an enzyme and the latter to a hormone. By utilizing the information obtained from these sources it was easy to construct an interesting theory of hypertension that implicated the parathyroid gland. In order to test the soundness of this theory, we decided to make use of parathyroid preparations in some cases of hypertension. From work published by Major, (9) it is known to us that the same relationship of the parathyroid to hypertension received consideration by him. He reports ten control experiments in which he used Hanson's parathyroid preparation intravenously in five dogs and Collip's in

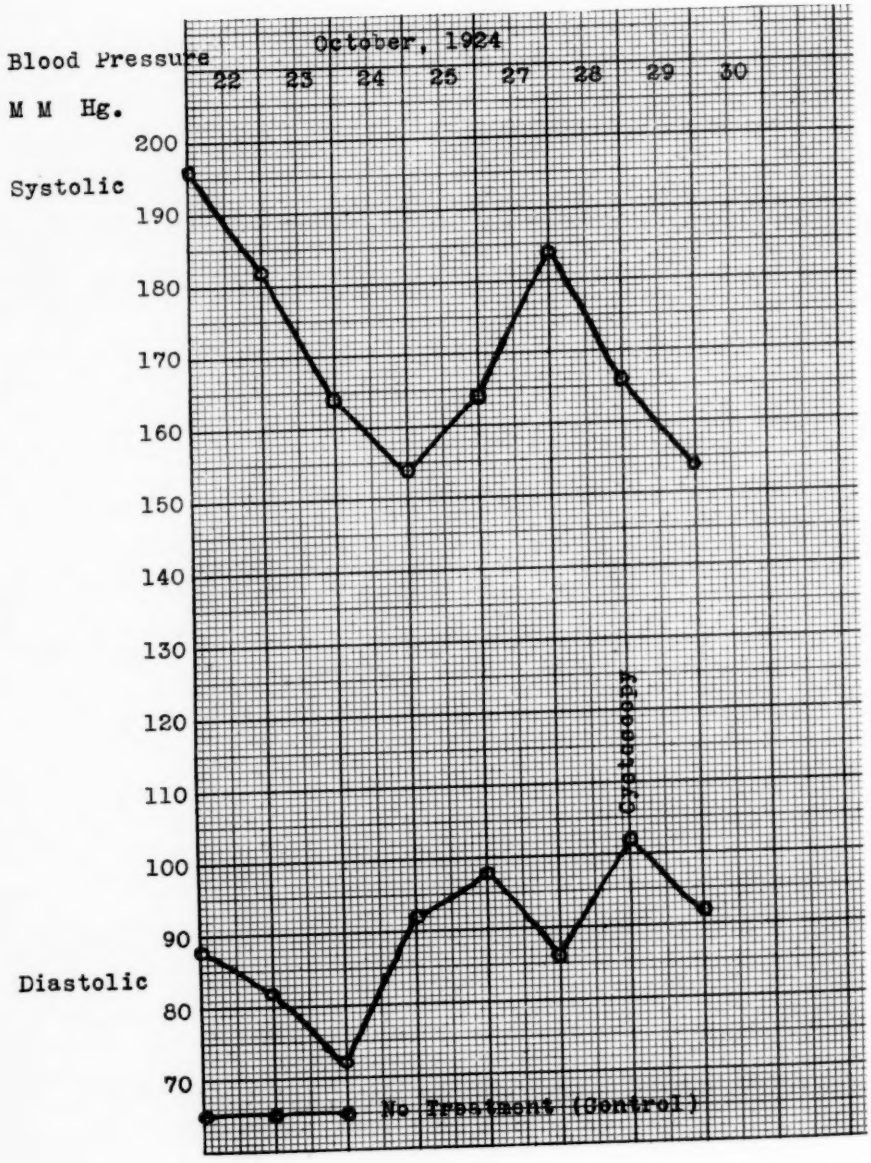

October, 1924
Blood Pressure
M M Hg.
22
23
24
25
27
28
29
30
200
190
180
170
160
150
140
130
120
110
100
90
80
70
Systolic
Diastolic
Captopril
No Treatment (Control)

FIG. 4

five others. It was found to have no effect on normal blood pressure, but when the experiments were repeated in animals with blood pressure raised by injection with methylguanidin, a prompt fall in blood pressure was produced with both preparations. These results are of interest to us, since the parathyroid preparation that we used in our observations for intramuscular injection was obtained from Hanson.

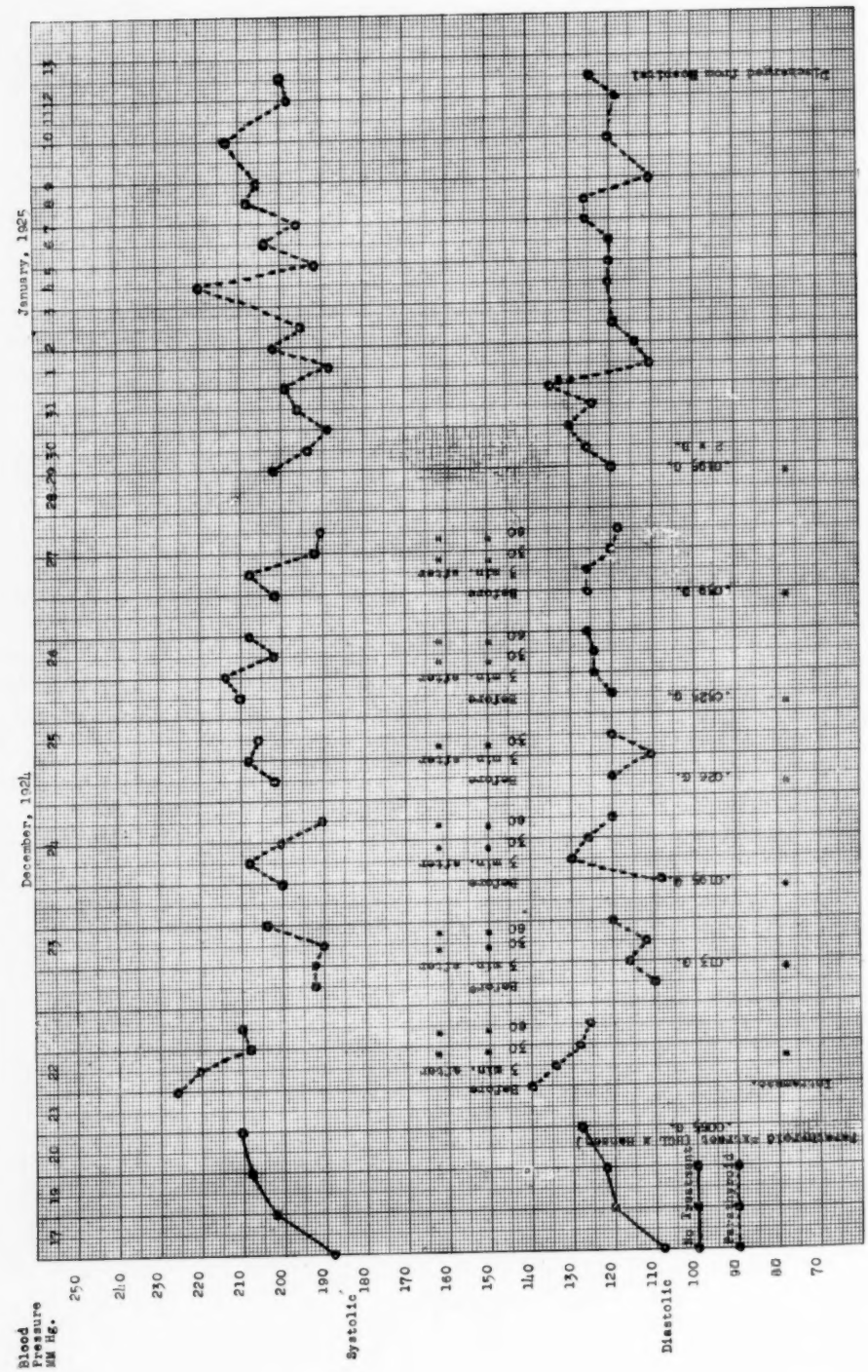
In our observation of parathyroid administration in clinical hypertension, we used Parathyroid Extract .0065 G. (Lilly) four times a day orally and a solution (Hanson's Hydrochloric X Sicca) for intramuscular administration.

Vines (11) states that the maximum parathyroid effect by the oral administration of extract 1/10 grain (.0065 G.) is obtained in about eight days. We believe that this preparation has been effective clinically in chronic tetany and in other clinical states where it was desired to maintain normal blood calcium levels.

We were supplied with parathyroid for intramuscular injection through the kindness of Dr. A. M. Hanson. The method of preparation of this substance is described by him. (13) The potency of the preparation in raising the serum calcium in parathyroidectomized dogs is also demonstrated. (14) Hanson removed the parathyroid in four dogs, on which a previous normal serum calcium determination had been made, namely, 11 to 12 mg. The day after operation, a drop in serum calcium of 2 to 3 mg. took place. By two 5 c.c. intramuscular injections on the second and third days, the maximum rise obtained was 15.7 to 20 mg., 64 to 72 hours after the first injection.

Hanson claims for his preparation (15) that it detoxicates guanidin and that it raises the ionic calcium to normal. He suggests its use in varicose ulcer, chronic infections, dental caries and tetany. In his published writings he has not, to our knowledge, advocated its use in hypertension. We advised him of our intended use of his preparation and are indebted to him for suggestions as to dosage and frequency of administration.

We used parathyroid extract .0065 gm. by mouth in three cases of hypertension over a sufficiently long period to obtain its action, without any apparent effect on the blood pressure. Hanson's Parathyroid Extract HCl, X Sicca was used in three cases in increasing daily dosage until a maximum of .039 gm. was given, and this dosage was then maintained. Observations on the immediate and sustained effect on the blood pressure were made. For immediate effect, the blood pressure estimations were made before 3 minutes, and 30 minutes and one hour after injection. No constant immediate effect from the parathyroid was discernible. The small variations that occurred were within normal limits of blood pressure variation. In two of the three cases there did not appear to be any sustained depressor effect on the blood pressure. One record (Figure V) is reproduced, together with that of the third patient, (Figure VI) in which there appeared for a time to be a decline in blood pressure, but there followed a rather abrupt rise, while the patient was still receiving parathyroid.


December, 1924
January, 1925
Blood Pressure MM Hg.
Systolic
Diastolic
Pulse Pressure
Heart Rate
Respiration
Temperature
Blood Sugar
Urine Output
Urine Specific Gravity
Urine Albumin
Urine Sugar
Urine Acetone
Urine Diacetic Acid
Urine Indican
Urine Urobilin
Urine Bile
Urine Blood
Urine Casts
Urine Pus
Urine Epithelial Cells
Urine Crystals
Urine Bacteria
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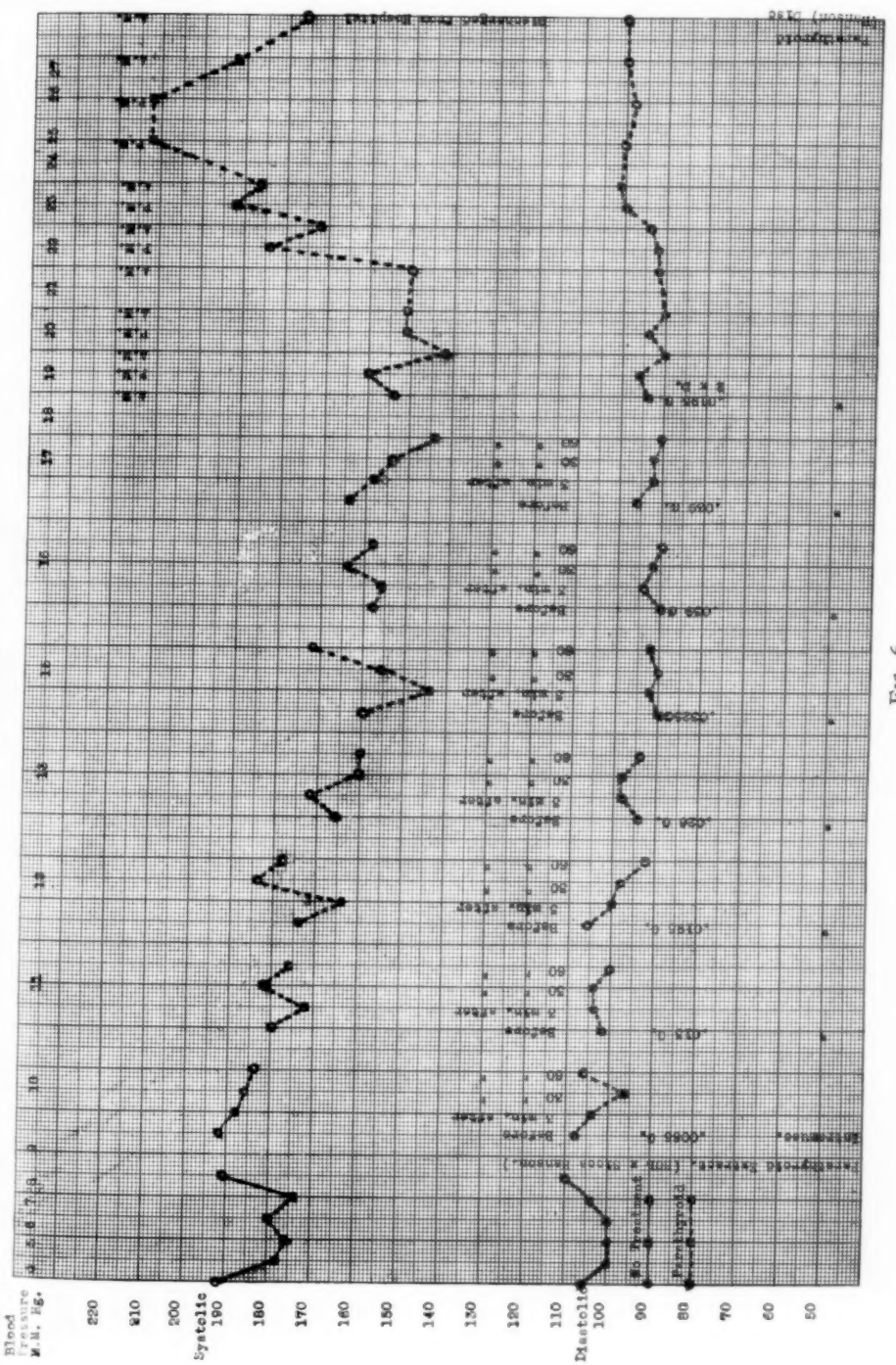

FIG. 6

We realize that it is not permissible to draw conclusions from the results obtained on the patients we had under treatment without a check on serum calcium. However, we gave both the calcium and parathyroid preparations in what are generally considered to be adequate dosages.

Our observations indicate to us that the problem of hypertension is still a more complex one than can be explained on the basis of a disordered calcium and guanidin metabolism. There apparently are other factors operative in its production, our knowledge of which at the present time is inadequate to explain its mechanism and manifestations.

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The Pathological and Clinical Significance of Congenital One-Sided Kidney Defect, With the Presentation of Three New Cases of Agenesia and One of Aplasia*

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Congenital one-sided kidney defect has been reported by many writers, beginning with Aristotle, because it has been considered a rare and interesting structural anomaly. Little attention was paid by the older writers to the clinical significance, probably partly because they considered the condition extremely unusual, and partly because many of the cases occurred in old people dying of other causes. The earlier reports, as well as some of the recent ones, are merely anatomical descriptions, without clinical data or description of other pathology found post-mortem. In the latter part of the nineteenth century with the development of surgery of the kidney, a number of instances of operative removal of a patient's only kidney, with the inevitable fatal result, attracted attention to that particular phase of the subject. Still more recently there has been some discussion of the possibility that such a malformation might render the individual more susceptible to kidney disease of various sorts and be a factor in influencing the prognosis in cases of pathology of the urinary tract. Four cases have occurred in the autopsy service of the University of Michigan which illustrate the types of cases found in the rather abundant literature which has accumulated on the subject. It is the purpose of this paper to present these cases together with the data gathered from a study of the recorded cases, which bears on the clinical importance of this condition, and to discuss the anatomical findings in such cases.

Obviously not all cases in which there is only one functioning kidney are analogous, either structurally or embryologically, and a grouping of cases is essential to any orderly discussion. One of the earliest is that of Rokitansky, (1) which, though it introduced terms which may be confusing, has influenced strongly all later classifications and has formed the basis for the naming of most recorded cases. He stated the situation as follows:

"When one kidney only is present, it is important to distinguish between the unsymmetrical and the solitary kidney. The former is represented by a

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right or left kidney, which is normal in regard to position and conformation, and occasionally rather enlarged, its fellow being deficient. The solitary kidney is the result of a fusion of the two organs, and therefore offers the characters peculiar to this arrangement in a greater or less degree. The lowest degree of fusion is seen in the horseshoe kidney (ren unguliformis); the two kidneys are united at their inferior portions by a flat riband-like or rounded bridge of tissue, which crosses the vertebral column. In the higher degrees the two lateral portions approach one another more and more, until they reach the highest degree, in which a single disk-like kidney, lying in the median line and provided with a double or single calyx, represents complete fusion."

For purposes of more accurate placing and elimination two other classes may well be introduced, giving four groups, as follows:

Class I. True one-sided congenital defect or agenesia, the "unsymmetrical kidney" of Rokitansky. By this it is understood that there is no tissue present on one side which can be grossly or microscopically recognized as kidney parenchyma.

Class II. Aplasia of one kidney. This group includes those cases in which atypical kidney parenchyma is present on one side on microscopic examination, but in which the development is so rudimentary that there is no functional kidney tissue.

Class III. Hypoplasia of one kidney, in which one kidney is much smaller than its fellow, but still exists as a functioning kidney.

Class IV. Various forms of fusion, the "solitary kidney" of Rokitansky.

Class V. Marked secondary atrophy or destruction of one kidney, not a disturbance of development.

Cases have often been listed without thorough study and classification, so that it is difficult to state definitely in which group a given case should be placed, and from a clinical point of view it often makes little difference whether a kidney is congenitally absent or destroyed by some secondary process. Of the four cases presented here three seem to fall in the first class, while the fourth might be properly placed in class two. Hence we shall be concerned only with agenesia and aplasia of one kidney, and in surveying the literature an effort has been made to exclude all those cases which represented a fusion or secondary atrophy, as well as those of hypoplasia. I have also endeavored to draw a distinction between the true agenesia and aplasia of one kidney, using the same criteria as will be pointed out in the discussion of the following cases.

Case I. *Aplasia of left kidney.*

A. B., age 5 months, male was admitted to the surgery service of the University Hospital January 14, 1917 for correction of a double hare lip and cleft palate. Preliminary wiring operations were performed on January 17 and and January 31. Early in March the child developed a severe diarrhoea and was transferred to the pediatrics service for treatment on March 19. The diarrhoea continued with much blood and mucus, the fluid output being apparently greater than the fluid intake. The child became very dehydrated and died on March 18, 1917. At no time during his stay in the hospital were there any symptoms indicating renal disturbance or insufficiency, and the case record

contains no note of anything in the child's past history pointing toward disturbance of kidney function.

Autopsy-96-U. Prosector: Dr. Weller.

The body is that of a poorly nourished male child showing to external examination bilateral cheilognathopalatoschisis, for which a preliminary plastic operation had been performed. The left pinna shows almost complete absence, and the right pinna shows a

Both adrenals were found in the normal location and appeared to be normal in structure.

The right kidney is large, measuring 7x4x2½ cm. The ureter is normal. On the left side is a soft flattened mass, lying in the usual location of the kidney, measuring 24x17x3 millimeters. This communicates with the bladder by a tubular structure having the appearance of a rudimentary ureter.

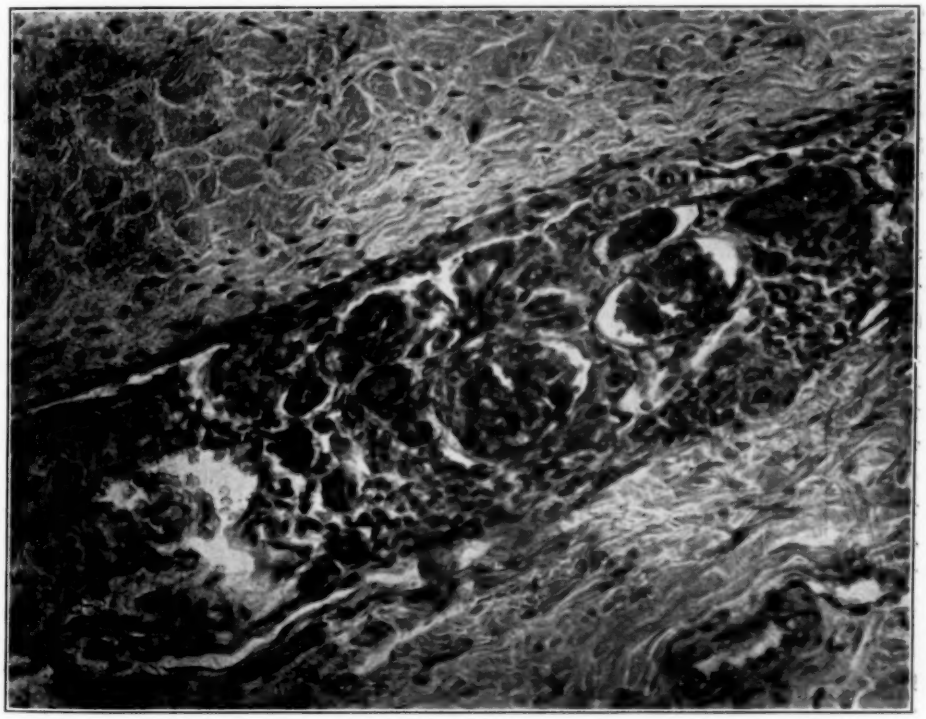

FIGURE 1. Photomicrograph of the aplastic kidney from Case I. There are a few glomeruli and tubules in a mass of dense fibrous tissue. Some of the glomeruli show obliteration. Haemalum and eosin stain, Zeiss AA ocular with number 4 compensating ocular.

similar condition in less marked degree. Both testes were in the scrotum. There is a small umbilical hernia.

On examination of the viscera the only anomalies outside of the genito-urinary tract were the occurrence of a Meckel's diverticulum measuring 9 cm. in length, located 60 cm. above the ileo-caecal valve, multiple diverticula of the colon, and a stenosis of the aorta at the isthmus.

There are no anomalies of the genital apparatus.

Microscopic examination of the kidneys: Dr. Warthin.

Right kidney: Numerous concretions of lime salts in the straight tubules, loops of Henle, and distal convoluted tubules. The convoluted tubules show hypertrophy. The nephrogenic zone is increased. Active new

formation of kidney tissue. Hyaline casts in many collecting tubules.

Left kidney: Is represented by a mass of hyaline connective tissue surrounding a cleft lined by flattened epithelium. At one pole there is a little group of glomeruli showing stages of obliteration and a few tubules.

Pathological Diagnosis:

Multiple anomalies. Bilateral cheilognathopalatoschisis. Meckel's diverticulum. Multiple diverticula of colon. Malformations of ear. Stenosis of aortic isthmus. *Aplasia of left kidney. Hypertrophy of right kidney with acute nephritis.* "Chalk infarcts." Renal insufficiency. Lymphoid exhaustion. Hypoplasia of adrenal medulla. General passive congestion.

This case represents a high degree of aplasia and no doubt many of the recorded cases in the literature of congenital absence of the kidney with the presence of the corresponding ureter and no microscopic examination of the tissue around the ureter must belong in this group. However, with the presence of tubules and glomeruli, no matter how rudimentary, this must be classed as an aplasia rather than an agenesia. A photomicrograph of this kidney is shown in figure 1.

Case II. *Agenesia of right kidney with persistence of right ureter. Associated genital malformations.*

Mrs. A. E., age 68, was admitted to the University Hospital May 21, 1926, as an emergency, after being struck by an automobile. A fracture of the skull was demonstrated by X-ray, but since there was no evidence of pressure and since the fracture was not compound no operative procedures were undertaken. The patient was unconscious for some days, and during the period following her recovery of consciousness she was irrational at times. During the routine physical examination a carcinoma of the left breast was discovered. Otherwise there were no findings of importance.

During her stay in the hospital the patient developed a toxic erythema for which no cause was demonstrated. On July 3 there was a sharp rise in temperature and the patient became comatose, dying on July 5, 1926.

No clinical findings are noted pointing toward an impairment of kidney function. A catheterized specimen of urine was negative except for the occurrence of 300-400 white blood cells per low power field of the microscope.

Autopsy 3-AE. Prosector: Dr. Fortune. Gross description of the genito-urinary system.

The right and left adrenals were found in their normal locations. The adrenal arteries and veins on the two sides were isolated and found to be without abnormality. The adrenals are of usual size, the cortex showing lipoidosis, but otherwise they are negative to gross inspection.

The left kidney was found in its normal location. Its vessels were dissected out and found to be normal. There is slight hypertrophy of this kidney, the measurements being 12x6x6 cm., and the weight, with some of the fatty capsule which was very adherent, was 210 grams. There is a very abundant fatty capsule which was removed with difficulty. The fibrous capsule stripped with ease leaving a smooth surface, showing a slight suggestion of foetal lobulation. Section showed a normal relation between cortex and medulla. The pelvis is of normal size and shape, and shows no evidence of inflammation. The ureter is of normal size and patent throughout. The ureteral orifice in the bladder is normally located in respect to the trigone.

At the corresponding level on the right no kidney could be found. No renal artery is given off from the aorta and no renal veins could be demonstrated. Nothing could be found in the usual location representing ureter, and there is no ureteral orifice in the bladder on the right side and the right half of the trigone is undeveloped.

There is a tubular structure terminating on the right side of the vagina about 5 mm. below the cervix uteri and arising in a tapering end 11 cm. higher at about the level of the brim of the lesser pelvis. This tube has

an external diameter at its lower end about equal to that of a lead pencil and its wall is about 2 mm. in thickness. It arises and ends blindly. Pieces were taken for microscopic study from the tapering end and from lower down.

The body of the uterus is distinctly divided into two cornua. The lesser of these is on the right and measures 3 cm. in length. The left horn is 4 cm. in length. The Fallopian tubes arise from the extremities of these cornua and show no thickening or dilatation. They both show an equal degree of development. The ovaries are of equal size. Both are wrinkled, firm and pale in color.

The peritoneum reflected from the right horn of the uterus forms a transverse band extending back to the rectum and roofs over about half of the pouch of Douglas.

The vagina shows no septum. The walls are smooth, rugae are not well marked. The cervix uteri is patulous and the little finger is readily passed in to the point of bifurcation of the body. No septum is present.

An anomalous artery arises from the anterior surface of the aorta 4 cm. above the bifurcation and distributes over the posterior surface of the rectum.

Microscopic examination of kidney, adrenals and anomalous tubular structure to right of vagina: Dr. Weller.

Adrenals: Of about normal size. Moderate patchy lipoidosis. Numerous small foci of mononuclear infiltration in the cortical portion. One adrenal shows accessory adrenal cortical tissue outside the capsule. This occurs in two forms: as spherical encapsulated nodules such as are usually seen, and as a diffuse intermingling of adrenal cortical cells with periadrenal fat.

Left Kidney: Moderate hypertrophy. Many large glomeruli. Numerous foci of active inflammation, chiefly near the capsule, and practically always centering about a scarred glomerulus. In some of the loops of Henle and straight tubules there is a deposit of a brown granular substance,—hemosiderin.

Anomalous Tubular Structure to the Right of Uterus and Vagina: This is a dilated tubular structure having a muscular wall. The musculature is not definitely arranged in layers, much of it running obliquely, although this differs in different levels. In one portion there is a well defined inner circular layer and obliquely running outer layer. The epithelium is of a transitional type, showing 2 or 3 layers of somewhat irregular columnar cells capped by larger flattened cells. The dilated lumen contains a mass of pink-staining albuminous material containing desquamated epithelial cells. Through this mass there are peculiar oval and cylindrical bluish staining bodies, probably older epithelial hyaline. In the muscular wall there are glandular structures in which these hyaline masses appear to form. These gland-like structures have epithelium somewhat like the main lumen and may be diverticula from it.

Pathological Diagnosis:

Fracture of skull in left occipito-temporal region. "Traumatic hemorrhagic encephalitis." Marked aortic and coronary atherosclerosis. Partial coronary occlusion. Myocardial fibrosis. Subepicardial fatty infiltration. Subendocardial fatty degenerative infiltration. Advanced scirrhous adenocarcinoma of left breast with metastasis to axillary lymph nodes. Chronic catarrhal bronchitis with acute purulent exacerbation. Chronic atrophic catarrhal gastro-enterocolitis. Old tuberculosis of bronchial nodes. Chronic purulent cholecystitis. Localized chronic parenchymatous hepatitis. Chronic hypertrophic purulent cystitis. *Multiple anomalies of genito-urinary tract (agenesia of right kidney and upper segment of right ureter, malposition of lower right ureter, bicornuate uterus with hypoplasia of right cornua, heterotopia of adrenal cortex in periadrenal adipose tissue). Moderate compensatory hypertrophy of left kidney with scattered foci of chronic inflammation.* Adenomatous colloid goiter. Fatty atrophy of pancreas. Lipoidosis of adrenals. Congestion, oedema, and parenchymatous degeneration of all organs.

The condition as regards the kidney in this case differs from the preceding only in the absence of the tubules and glomeruli. The question may well arise whether the gland-like structures found

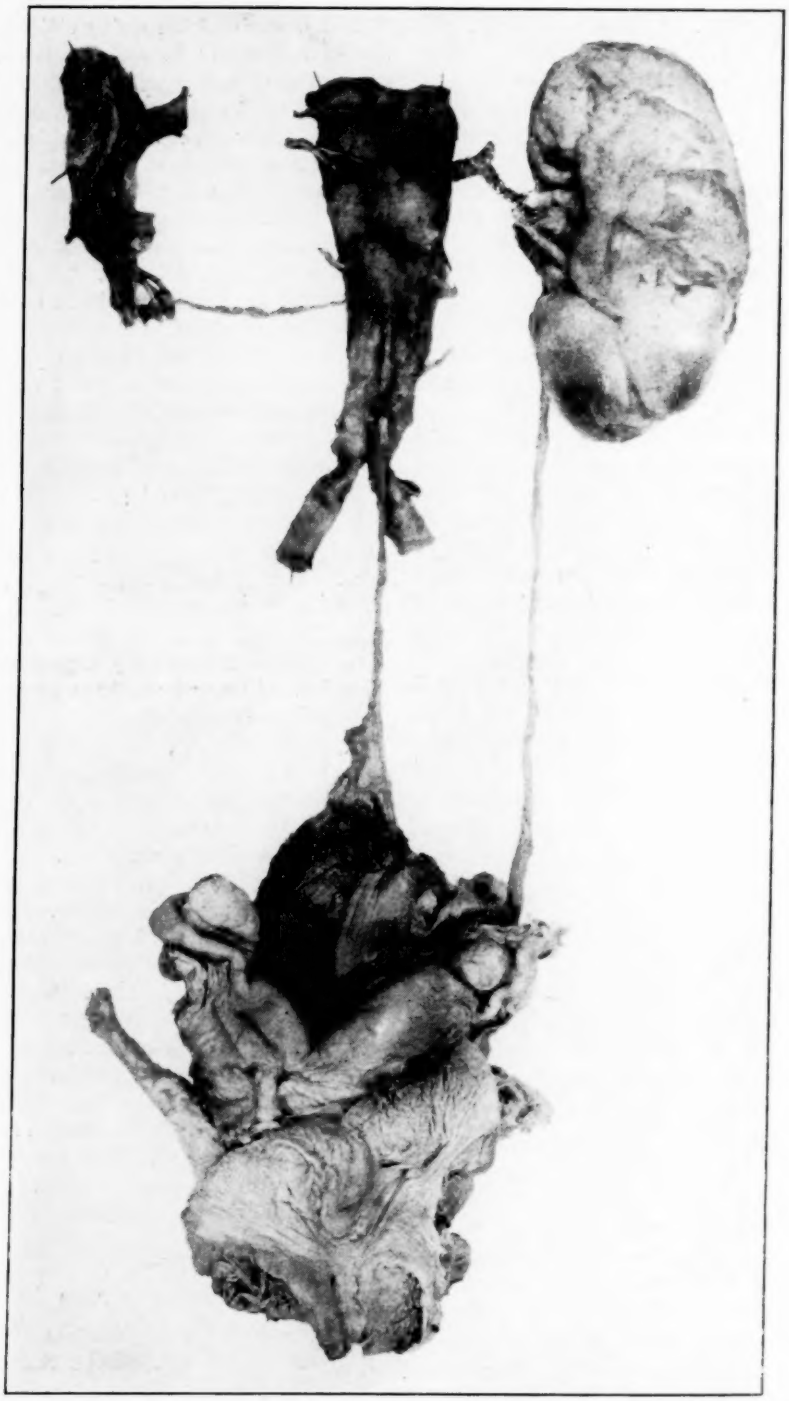

FIGURE 2. Gross preparation of the genito-urinary tract from Case II. The right kidney and vessels and the right ureteral orifice in the bladder are absent. A rudimentary ureter is seen arising to the right of the vagina. The bicornuate uterus shows a poorly developed right horn.

around the ureter-like tube are kidney tubules and whether this should not be classed as a case of rudimentary kidney. However, the microscopic appearance of the epithelium indicates that they should be considered as a part of the ureter, perhaps as rudimentary calices, and hence this case was classed as a true agenesia. Certain writers, notably Aschoff (2) state that in agenesia of the kidney the ureter is always absent and would include all such cases as this as aplasia of the kidney. Since the ureter and kidney are not inseparably linked embryologically, as will be pointed out later, there seems no reason why the ureter cannot exist without the kidney and most of those who have written on this subject are willing to admit such a possibility. These cases serve to show how readily one condition grades over into the next more severe and how difficult a classification may sometimes become. The associated genital malformations in this case are very interesting and also quite common findings. Their occurrence and significance will be discussed more fully later. A photograph of the intact urogenital system is shown in figure 2, while figure 3 is a photomicrograph of the rudimentary ureter.

Case III. *Agenesia of left kidney, ureter and adrenal. Associated genital malformations.*

I. C., female, age 15, was seen in the outpatient department of the University Hospital April 11, 1923 on refer from a school physician with question of thyroid disturbance. A diagnosis of simple colloid goiter was made and there is nothing in the case record to indicate that she presented any evidence of disturbance of kidney function. She was admitted to the hospital at 4 p. m. on September 18, 1923 in a stuporous condition. Her father stated that she had been well until three days previous, when she scratched a boil on the right cheek. On physical examination a crusted area was found in the middle of the right cheek. The whole right side of the face and neck was swollen and reddened. The skin of the entire body was ashen except for cyanosis over the extremities. The pulse was irregular and rapid. Breathing was shallow and rapid. There were no signs of meningitis. She died at 8 p. m. on the day of admission. The only laboratory examination made was a blood culture, which was positive for streptococcus hemolyticus.

Autopsy 39-AB. Prosector, Dr. Hall.

Gross description of the genito-urinary system: Examination of the location normally occupied by the left adrenal showed no tissue suggestive of adrenal. The right adrenal is of normal size and shape and in the normal location.

In the usual position of the left kidney there is only a mass of fat, which on microscopic examination showed no trace of kidney structure. The left ureter is also totally absent.

The right kidney is slightly larger than normal, measuring 15x6½x3½ cm. The fatty capsule is fairly abundant and stripped readily. The fibrous capsule stripped readily, leaving a surface smooth, except for foetal lobulation. The right ureter is of usual size and shows no variations from normal.

The uterus is unicornuate in type. The right horn is well developed and attached to this is a tube and ovary of normal appearance. The left horn shows no development whatever and the left tube which is rudimentary is attached to the wall of the pelvis by a rudimentary broad ligament and neither tube nor ligament have any connection with the body of the uterus. In connection with this rudimentary tube is a small ovary, described as being the size of a large bean, but with a hemorrhagic cystic Graafian follicle the size of an olive arising from it. The hymen is unruptured and normal in appearance. The vagina is of a normal virginal type and shows no septum.

Microscopic Examination *Right Kidney*: Dr. Warthin.

Passive congestion and slight cloudy swelling. Metastatic abscesses with central colonies of cocci plugging the vessels. Excretory abscesses in the pyramids. No evidence of hypertrophy in the microscopic section.

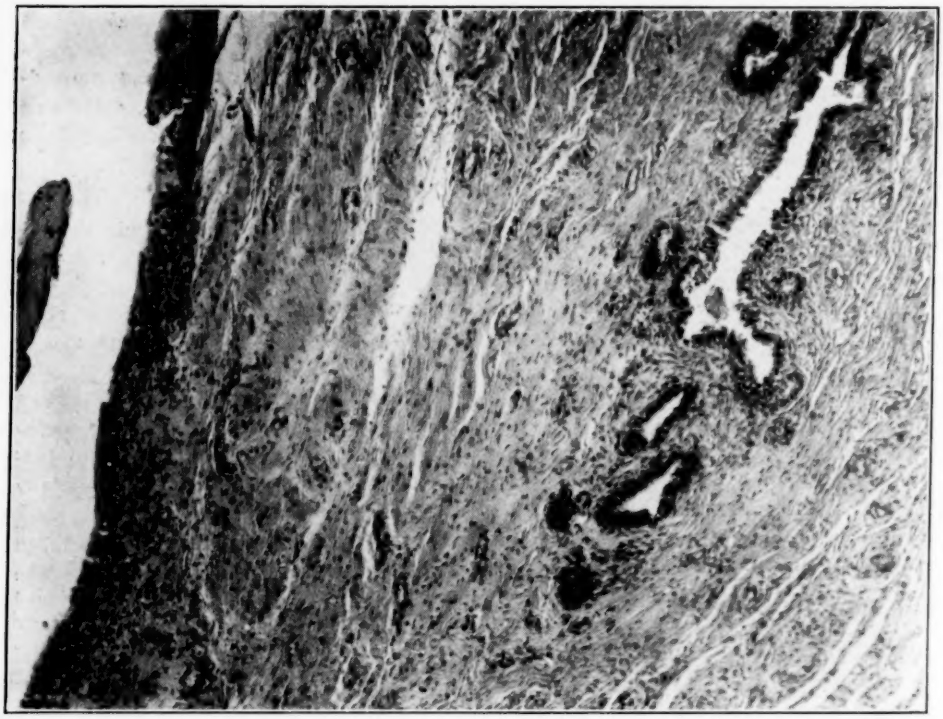

FIGURE 3. Photomicrograph of the upper segment of the rudimentary ureter from Case II. The tube is lined by an epithelium of a transitional type, and its lumen contains a mass of pink staining albuminous material. In the muscular wall is seen a gland-like structure lined by epithelium of the same type as in the main lumen. Haemalum and eosin stain, Zeiss AA objective without ocular.

Pathological Diagnosis:

Septico-pyemia. Multiple pyemic abscesses in thyroid, heart muscle, lungs, kidneys, and liver. Diffuse phlegmon of the right side of the face, right orbit and upper portion of the right side of the neck, following a furuncle on the right cheek. Acute passive congestion and parenchymatous degeneration of all organs. *Anomalous development of left urogenital tract. Agenesia of left kidney, ureter and adrenal. Aplasia of left ovary, tube and broad ligament. Unicornuate uterus.* Thymico-lymphatic constitution.

This case represents one of the most complete defects of the urinary tract seen in the female. The similarity of the genital anomalies to those of the preceding case will be noted, but as the urinary defect has become more complete, the lack of development of the genitals on the corresponding side has become more pronounced. The abscence of the adrenal is, as might be expected, a rather common finding in such cases.

Case IV. *Agenesia of left kidney and ureter. Associated genital malformations. Heterotopia of right adrenal in kidney.*

G. M., age 21, single, entered the University Hospital December 9, 1926 with the chief complaint of impairment of vision for six weeks. Three years previous to his admission he was examined and passed for life insurance. A year and a half later he was again examined for life insurance, but at this time the systolic blood pressure was 230 and albumin was found in the urine. He gave a doubtful history of a discharging ear in infancy, boils on the neck three years, and a pharyngeal abscess two years before admission. He had noticed no edema, dizziness, or headache, but he did complain of shortness of breath and failing appetite, also a loss in weight of 15 pounds in one year.

Physical examination showed marked enlargement of the heart, the cardiac apex extending 13 cm. to the left of the midsternal line. There was a pericardial friction rub near the apex. Visible pulsation of the carotid arteries was noted. The blood pressure was 240/140. The optic fundi showed the characteristic changes of chronic nephritis. There was no edema or ascites noted.

Laboratory tests showed the urine to be acid with a sp. g. 1.010, albumin 4 plus, and a few finely granular casts. On December 10 there was no elimination of phenol-sulphone-phthalein in two hours. The non-protein nitrogen of the blood rose from 84.5 mgs. per 100 c.c. on admission to 210 mgs. per 100 c.c. four days later. A concentration test gave a variation in the specific gravity of the urine from 1.010 to 1.013.

On December 13 pleural friction rubs and râles in the lung bases were heard. The patient became stuporous and died on December 14, 1926.

The clinical diagnosis was chronic nephritis, hypertensive heart disease, lobar pneumonia, and cardiac failure.

Autopsy 129-AE. Prosector: Dr. Fortune.

Gross description of genito-urinary system.

The abdominal aorta, inferior vena cava, adrenals, right kidney and pelvic organs were removed en masse.

Upon dissecting away the adipose tissue the right adrenal is found in its normal location. It is of normal size but very much flattened having the contour of a slightly irregular disc. It receives its blood supply from an artery arising from the aorta just lateral to the superior mesenteric artery and is drained by a vein emptying into the vena cava just opposite to the renal vein of the opposite side. These vessels are surrounded by sympathetic ganglia of the coeliac group, and hemolymph nodes.

No kidney can be found on the left side nor anything suggestive of kidney anlage. No artery arises from the aorta to correspond to the left renal artery and no vein empties into the vena cava to represent the left renal vein. A small artery arises from the aorta just below the left adrenal artery and terminates in the mass of sympathetic ganglia and hemolymph nodes. Microscopic sections of this area showed nothing suggestive of kidney tissue.

No ureter, nor anything suggestive of rudimentary ureter, could be found on the left side and the bladder contains no ureteral orifice on the left side. The left half of the trigone is undeveloped.

The right adrenal was found in its normal location. It is also markedly flattened and has the form of an oval plaque, slightly larger than that on the left. It receives its blood partly by an artery from the aorta distributing to it alone and partly from another artery distributing partly to it and partly to the superior pole of the right kidney. It is drained by a vein emptying into the inferior vena cava. The adrenal is very closely joined to the kidney and grossly there appears to be at least a fusion of the two capsules, if not an actual heterotopia of adrenal into kidney substance.

The right kidney averages 11 x6 x4 cm. The capsule stripped with great difficulty showing a tendency to splitting. The surface left is very granular, the granules averaging about 2 mm. in diameter. On section, the kidney cortex is found to average 5 mm. in thickness. The pelvis is dilated and moderate congestion of the mucosa is present. The kidney parenchyma appears swollen with

decreased translucency—a picture suggesting cloudy swelling. The whole is indicative of a marked secondary contraction of a previously hypertrophic kidney. The right ureter is dilated, averaging 1 cm. in external diameter. It opens into the bladder by a normally located ureteral orifice.

The right seminal vesicle was found in its normal location. It is of usual size. On section, it was found to contain a turbid fluid resembling semen. The right vas is in normal location. It is not thickened, and in no way appears abnormal.

On the left side no seminal vesicle or vas deferens could be located, although the bladder was dissected entirely from the rectum. The prostate is small and firm. It is slightly asymmetrical, there being a pea sized accessory lobe in about the usual location of the left seminal vesicle. No unusual appearance was found on section. The ejaculatory duct on the right side is normal in appearance. No ejaculatory duct could be located on the left.

The right testis is of normal size. On section, there is the usual granular appearance of the body. The epididymis arises at the usual location. It is of normal size, shows no evidence of pathology. The right vas arises at the normal location.

The left testis is of about the same size as the right. On section, the parenchyma is slightly less granular than on the right, but there is no marked gross difference. The epididymis arises at its usual location by seven vasa efferentia. The epididymis is, however, only seven centimeters in total length and becomes rapidly smaller toward the end. It terminates in a fibrous strand which attaches alongside the vasa efferentia as they arise from the mediastinum testis. No vas deferens arises from the epididymis.

Microscopic findings bearing on the renal condition: Dr. Warthin:

Heart: Advanced coronary atherosclerosis. Hypertrophy of heart muscle with secondary atrophy and diffuse fatty degenerative infiltration. Marked increase in stroma throughout the heart. Patches of sclerosis are present in the left ventricular wall. Endocardium shows sclerosis. Marked subepicardial fatty infiltration with serous atrophy.

Aorta: Well advanced atherosclerosis.

Right Kidney: Late stage of chronic glomerulo-tubular nephritis. Advanced contraction. Right adrenal shows heterotopia into kidney cortex beneath the capsule. There is marked sclerosis of the renal vessels, secondary to hypertrophy. Some vessels show obliterating endarteritis.

Both testes: Aspermatogenesis. Congestion and oedema.

Pathological Diagnosis:

Agenesia of left kidney and ureter, left seminal vesicle and vas. Advanced glomerulo-tubular nephritis of right with marked contraction. Heterotopia of right adrenal into kidney cortex. Right-sided hydroureter and chronic pyelitis. Cardiac hypertrophy and dilatation. Cardiac insufficiency. Brown induration of lungs with marked edema, congestion and emphysema. Wet brain and meninges. Hydrothorax, hydropericardium and ascites. *Advanced atherosclerosis of renal and coronary arteries and aorta.* Fatty infiltration of heart and liver. Colloid goiter. Colloid cyst in pituitary. Atrophy, passive congestion and parenchymatous degeneration of all organs. Chronic stasis catarrh of gastro-intestinal tract. Lipoidosis of adrenals.

The anatomical features of this case correspond very closely to those of the preceding case except for the sex difference and the presence of the adrenal in case IV. It is difficult to state just what, if any, significance should be attached to the heterotopia of the right adrenal in the kidney substance. Very few instances are reported in connection with absence of the other kidney. The significance of heterotopia of the adrenal in kidney and liver has been discussed by Weller (3) and he concludes that the condition is usually found in cases of constitutional pathol-

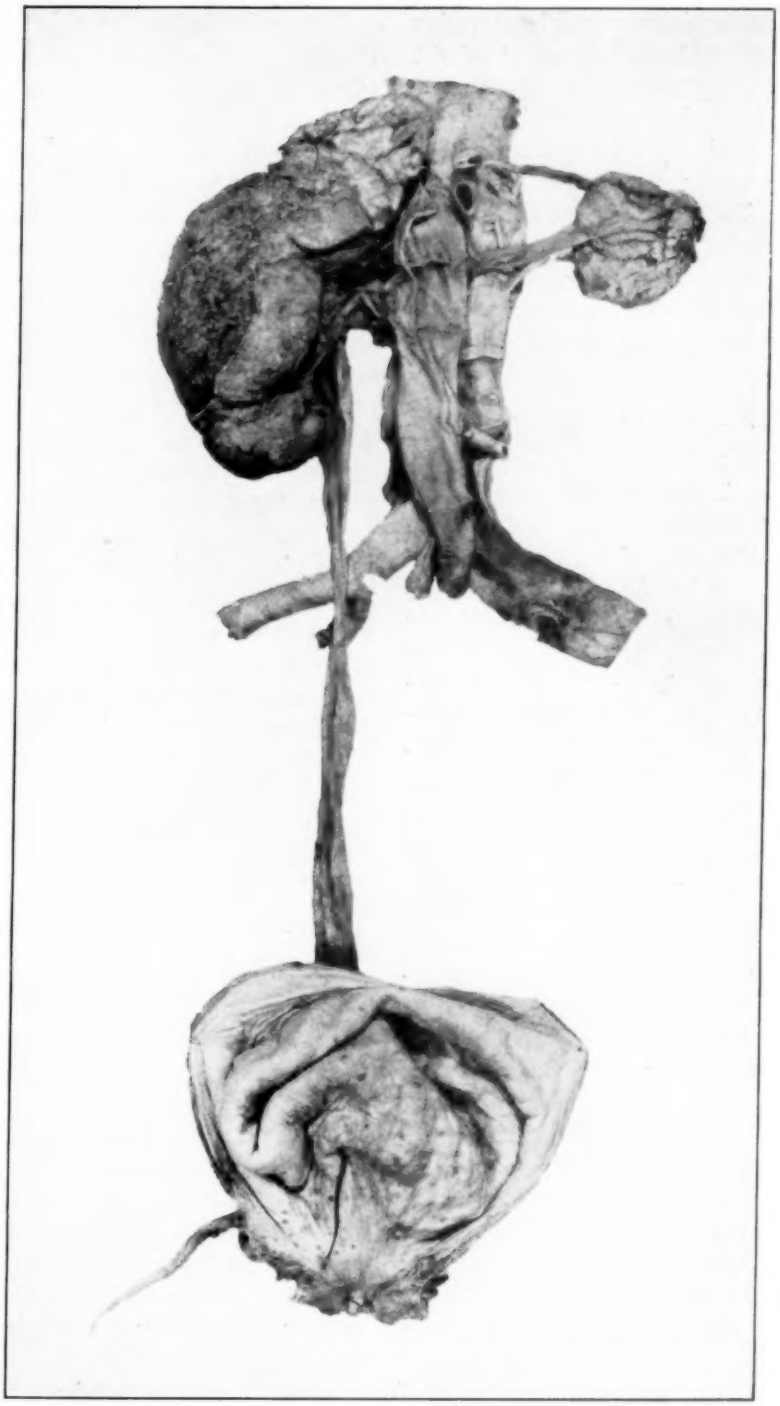

FIGURE 4. Gross preparation of the genito-urinary tract from Case IV. Both adrenals are present. The left kidney, renal vessels, ureter, seminal vesicle, vas deferens and a portion of the epididymis are absent. There is only one ureteral orifice in the bladder. The right kidney shows marked secondary contraction.

ogy and there is no especial connection between it and malformations of the genito-urinary tract. Its occurrence in this case probably has no significance other than that we are dealing with a constitutionally pathologic individual. The significance of the genital malformations will be discussed later. Figure 4 is a photograph of the intact urogenital system from this case and figure 5 shows the malformation of the epididymis.

Evidence as to side most frequently involved:

The available recorded cases of congenital one-sided kidney defect have been studied and of these 422, including the three listed above, were considered to be true agenesias of the kidney while two recorded as congenital absence of one kidney seemed definitely to fall in the class of aplasias. Only those cases were included where autopsies had been performed. Several cases reported as rudimentary kidney were excluded on the ground that from the description it appeared that the case was one of a hypoplastic but functional kidney. It is probable that in many of the reported cases, if careful microscopic examination had been made of the tissue in the region normally occupied by the kidney, the group of aplastic kidneys would have been increased at the expense of the group of true agenesias, but unfortunately in many of the cases such evidence is lacking. Of these cases the side of the kidney defect was noted in 387 cases, in 218 of which it was the left and in 179 the right. This proportion agrees in a general way with that found by other writers, which is interesting in view of the fact that Aschoff states it is not yet definitely decided which side is more frequently involved. Ballowitz (4) in 1895 collected 213 cases of which 117 were on the left and 88 on the right and in 8 the side not stated. Gerard (5) in 1905 in a series of 278 cases says that the kidney was stated to be absent on the left in 109 instances and on the right in 76 cases. He further states that in his series 78 males showed an absence on the left and 44 on the right as compared with 31 females showing an absence on the left and 32 on the right. Winter (6) observed the condition 129 times on the left and 98 times on the right in a series of 237 cases and noted the same preponderance of the male sex for a left-sided defect. In my own collected series the preponderance of the male sex for the left side is in the ratio of 116 to 82, while the female sex shows a ratio of 87 to 79 in favor of the left side. Thus if the individual is a male the chances are strongly in favor of a left-sided defect, while in the female there is no preponderance in favor of either side.

Condition of the existing kidney:

The presence or absence of hypertrophy in the existing kidney has called for much consideration and in 195 of the 422 cases which I have collected this condition was noted. The degree of increase varies from "slight hypertrophy" to kidneys described as three times normal size. In some of these extreme cases, one wonders whether a part of the increase can not be explained on the basis of extreme congestion or some other pathologic condition. The increase in size is reported in most cases where microscopic examinations have been done, as being due

to hyperplasia, rather than a hypertrophy of the glomeruli and tubules. In most of the cases the kidney is reported as being of normal contour, although occasionally there is some distortion in the shape. Fetal lobulation does not appear to be noted in more instances than would be expected in an average run of cases. Much emphasis has been placed by some writers on the importance of a misplaced kidney in diagnosis of congenital one-sided defect, probably influenced by Polk's (7) famous case of removal of a single pelvic kidney. In my series only 20 cases showed a misplaced kidney, indicating that the condition is not frequent enough so that one is justified in expecting a misplaced kidney in these cases. Heiner, (8) who has fully discussed the subject of renal dystopia, concludes that renal dystopia is much more apt to be present where there is a congenital one-sided kidney defect than where both kidneys are well formed, so that in cases of misplaced kidney one may well be on the lookout for a congenitally absent kidney.

Presence or absence of the ureter:

The condition of the ureter on the affected side is an interesting phase of the subject. In 228 of my collected series of 422 or 54% of the cases, it was noted as absent, while in 42, or 10%, it was noted as present. In the remainder of the cases no mention is made of it. In 104 cases the ureteral orifice in the bladder is stated to be absent on the affected side. In several cases the site of the ureteral orifice was marked by a slight depression or even by a small diverticulum. Where no ureteral orifice is present on the side of the defect, the other orifice is usually in its normal location and there is an asymmetry of the trigone. The ureter when present usually has no lumen or a lumen only part of its length and feathers out at its upper end, although in some cases a slight swelling is reported at the upper extremity. In some of these cases no microscopic examination of this swelling has been made, and it is possible that if this had been done these cases would be properly classed as aplasia. In other cases, this swelling has proved to be made up of connective tissue only.

Renal vessels and adrenal:

The absence of renal vessels on the side of the absent kidney has been noted in 100 cases of my series from the literature, and in many of those where vessels were present, they were simply small twigs distributing to the connective tissue, sympathetic ganglia, or sometimes to the adrenal on that side. In 46 cases of the 422 the adrenal was stated to be absent. When described as present it is usually of approximately normal shape although sometimes enlarged and flattened.

Proportion in males and females with discussion of associated genital defects:

All statistics show this condition to be more common in males than in females, statistics varying up to 4 to 1. My series shows a marked variation from this in that of the 381 cases where the sex was stated 198 were males and 183 females. Perhaps one explanation of this lies in the fact that the commonness with which deformities of the genital tract accompany this

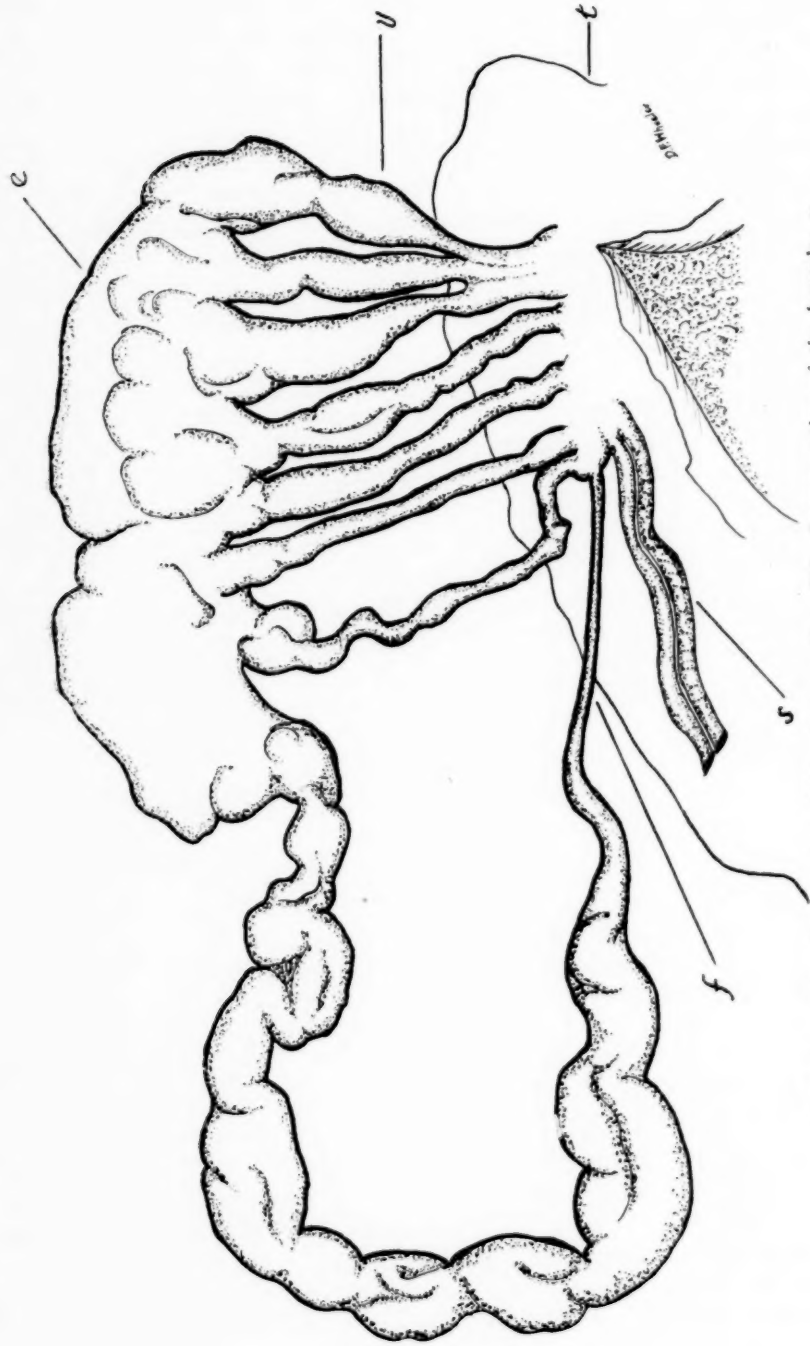

FIGURE 5. Dissection of the epididymis from Case IV. Interpretation of the legends: *v*, vasa efferentia arising from mediastinum testis; *e*, body of epididymis; *f*, fibrous cord marking termination of epididymis and attaching alongside mediastinum testis; *s*, spermatic artery and vein; *t*, body of testis with tunica albuginea opened one one side.

condition in the female lends interest to female cases and leads to a greater frequency in the reporting of such cases. In my series 128 of the 183 female cases showed serious malformations of the genital tract. Eismayer (9) in 1923 collected 122 cases and classified them as to the type of defect. The commonest forms are unicornuate and bicornuate uteri of varying degree of development, the horn on the side of the defective kidney being less well developed. Didelphic uterus, septate uterus, and even absence of the uterus also occur. Malformations of the ovary are not common, case III (vide supra) being rather unusual in that respect, although there are a few cases of absence of the ovary and also of dystopia of the ovary. Deformities or hypoplasia of the external genitals are rather common, and atresia of the vagina, absence of the clitoris, septate vagina, as well as malformations of the labia occur. Unusual terminations for a persistent ureter on the defective side are reported, both in the cervix and alongside the vagina.

Genital deformities in the male are less common than in the female, only 42 cases out of the 198 in my series stated to be male sex showing them. The commonest type of malformation is similar to that described in case IV (vide supra), although there are several cases of a rudimentary seminal vesicle on the affected side with a persistent ureter terminating in it, as well as cases of termination of a rudimentary ureter in the vas deferens. The testis is reported present on the affected side in all my cases, but often it is less well developed than its fellow, and occasionally is undescended.

Embryological factors:

The frequent association of renal agenesia and genital malformations naturally leads to a consideration of the closely linked embryology of the two systems. In this connection it must be remembered that the human being develops three distinct sets of excretory apparatus. The first of these, the pronephros, furnishes the duct system for the second organ, the mesonephros, but otherwise disappears entirely. The mesonephros, or Wolffian body, gives rise to important structures in the male, which are from cephalad to caudad, the efferent tubules of the testis, the vas deferens, the ejaculatory duct and seminal vesicles. The third excretory organ or metanephros develops as a budding off from the mesonephros and forms the anlage of the adult kidney. Simultaneously with this there develop two ducts known as the Müllerian ducts, which in the male give rise to no important structures, but in the female fuse caudad to form the vagina and uterus, and in their divided portion give rise to the Fallopian tubes. The sex glands arise separately from this duct system in a mass of tissue known as the genital ridge. The ureter arises as a bud from the Wolffian duct near its opening into the cloaca. The adrenal glands are linked in this development only by position, the cortex being of mesothelial origin while the medulla develops from the ectoderm of embryonic sympathetic ganglia.

Radasch (10) has pointed out that there are three possibilities of explaining renal agenesia: (1) A failure of the appearance of the metanephric bud, resulting in the absence of the kidney

even though the structures derived from the mesonephros were normal, (2) Appearance and early regression of the metanephros, (3) Failure of the pronephros, and therefore the mesonephros to appear. He reasons that since there is no uniform association of genital deformities, the first two propositions must explain absence of the kidney and that genital anomalies develop secondarily. While there can be no doubt that some cases of kidney agenesia can be explained by one of the first two theories, and cases of renal aplasia on the second theory, there is a fourth possibility which Radasch has overlooked, namely the appearance, but imperfect development of the mesonephros. Pohlman (11) discusses this possibility and advances the proposition that a failure of the Wolffian duct to unite with the cloaca may explain some of the combinations of anomalies which occur. This he argues would remove the stimulus for the formation of the metanephric bud and hence result in absence of the kidney and those structures in the male arising from the Wolffian duct.

Kornfeld (12), at the Institute of Embryology in Vienna, has carefully studied by serial sections a human embryo of 5 cm., vertex-heel length. He observed a complete left sided absence of the metanephric bud and the ureter and a deficient development of the Müllerian and Wolffian ducts, particularly in the caudal portions. Also there was no development of the left renal vessels. His embryo was a male, and from this he argues that if it had gone on to maturity there would have been absence of the left kidney, ureter, ejaculatory duct, seminal vesicle, vas deferens and a portion of the epididymis. It will be noted that this case is entirely analagous to case IV reported above. The developing testis was not involved in the malformation. The fact that genital defects in the male always are most severe near the bladder and may diminish toward the testis seems to lend strength to the theory that a disturbance in the caudal portion of the embryo involving the Wolffian duct explains such anomalies. The greater frequency of genital malformations in the female associated with absence of one kidney can be understood by remembering that the Müllerian duct represents a later development than the Wolffian duct, and hence its chance of being involved in malformations is greater. In this case also the commonest malformations are those of the caudal portions, the uterus and vagina, while the Fallopian tubes are usually less involved.

Association of multiple anomalies with kidney defect:

As in all cases of disturbance of development, there are often serious malformations in other portions of the body, but the occurrence of multiple malformations outside the genital tract is much less uniformly the case than with many other types of deformity. Of the four cases presented above, three were perfectly normal except for the urogenital system. Of the 422 cases collected from the literature only 32 or 8% showed serious malformation outside of the genito-urinary tract. Where malformation is present it varies all the way from such monstrosities as sirenomelia down to hare-lip as in the case from this series. One case

of situs viscerus inversus associated with right sided absence of the kidney is noted. Thus it follows that the average patient who has only one kidney will show nothing in his external appearance to indicate his anomaly if a male, since usually the difference in the size of the testes is not great enough to occasion any suspicion of a defect in vas or seminal vesicle. In females the frequent malformation of the external genitals might serve as a warning in those cases where vaginal examination is done, but even in females many cases present nothing to excite any suspicion either of a malformation of the inner genitals or the absence of a kidney.

Frequency of agenesia of the kidney:

In considering the clinical interest of such a condition one thinks at once of its frequency as influencing its importance. Most of the older writers considered it as so rare that it could have little clinical interest to the physician. Ballowitz (4) saw it once in 617 cases. Morris (13) collected the statistics from four London hospitals and found that in 15,904 autopsies the condition occurred six times, or once in 2,650 cases. Anders (14) found at Pennsylvania Hospital 1 case in 1250 and at Philadelphia Hospital 8 cases in 6,240 autopsies. Such figures might be listed at length and they vary from one case in 4,000 autopsies to two cases in a series of 47 autopsies. At the University of Michigan three cases of true agenesia and one of renal aplasia have occurred in 2,580 autopsies. By adding up a total of 21 large series reported we find 108 cases in 139,346 autopsies or a ratio of 1 case in 1290 autopsies. It is interesting, however, to note that two of the three cases of total agenesia reported in this paper occurred in a series of 128 autopsies and within six months of each other. This emphasizes the fact that while the condition is relatively rare it is not so rare as to preclude the possibility of it occurring in the practice of any physician.

Surgery of the unilateral kidney:

A considerable number of instances of complete anuria with death have followed operations on a single kidney. Polk's (7) case of the removal of a pelvic tumor which proved to be the individual's only kidney has already been cited. Winter (6) in 1901 removed a large cystic kidney which proved at autopsy to be the only one present and at that time he collected 10 other cases from the literature with operative total removal of a supposed single kidney and death. In four of these, including his own, autopsy was performed and the agenesia of the other kidney confirmed. Two cases of traumatic rupture of a congenital unilateral kidney with death have also been reported. Venzmer (15) in 1921 collected 19 cases of operation on a one-sided kidney, and discussed the danger of operations on the one-sided kidney. In my collected series of 422 autopsies there are ten deaths following removal of one kidney and also six deaths following other operations on the kidney. Of these four were attempts to remove calculi and two pyelotomies for drainage. The death was of uremic type and in two of the six cases a total anuria was noted. These facts indicate that any operative procedure on a

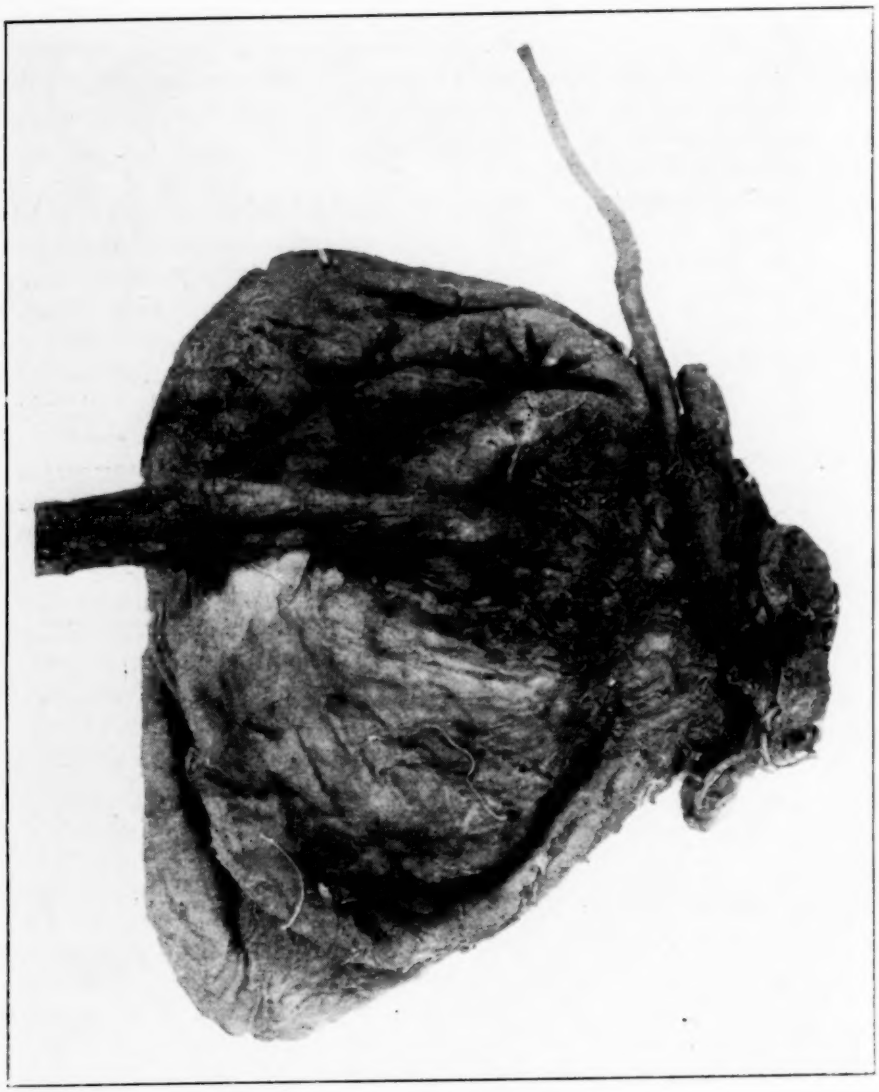

FIGURE 6. Detail of the posterior aspect of the bladder from Case IV. The left vas and seminal vesicle are absent and there is a small accessory lobe of prostate on the left side. The single, dilated ureter arises from the right side.

single kidney should be undertaken with caution. Against this there are at least five cases in the literature of complete anuria which was apparently due to obstruction of the ureter from a single kidney, successfully treated surgically. Of course in these cases one can only say that there was only one functioning kidney and that X-ray and other clinical means failed to demonstrate a kidney on the opposite side, but the clinical aspects of the case would not be altered by the presence of a rudimentary and non-functioning kidney. Of these operations, four were ureteral catheterizations and dilatation for stricture of the ureter, one of a ureteral transplant, and one the removal of a ureteral stone. The study of these few cases indicates that drastic operations on a single kidney are hazardous and should be undertaken only when more conservative measures are not applicable or have been inefficacious.

Occurrence of disease in a unilateral kidney:

Recently attention has been attracted to the frequency with which renal diseases occurs in cases of unilateral agenesia of one kidney. Anders (14) reported this finding in 46.5% of his cases. A study of my collected series of autopsy cases shows that renal diseases were mentioned in 96 instances or 22.6%, less than half the instance reported by Anders. Part of the variation may be explained by the fact that my series included a considerable number of cases overlooked by Anders and reported in anatomical journals as anatomical curiosities. In practically none of these is the presence or absence of renal disease in the existing kidney noted, so that if the data had been complete undoubtedly my percentage would have been higher. Of these 96 cases 28 had some form of chronic nephritis, 23 stone in the kidney or ureter, 35 some other serious kidney diseases, pyonephrosis, hydronephrosis, tuberculosis, purulent nephritis etc., while in 10 cases the kidney disease was more or less incidental. While it is recognized that such a procedure has little statistical value, in order to get some basis of comparison a similar series of 422 autopsies from the files of the Department of Pathology of the University of Michigan were reviewed and 64 cases of kidney disease were found or 15%, of which 17 mentioned the kidney disease as an incidental occurrence. Thus without considering the fact that probably the percentage of cases of kidney disease in the cases collected from the literature is low, the percentage of kidney disease is a half greater in cases of one-sided defect than in a normal run of autopsy cases. It must be recognized of course that many of the individuals with a one-sided kidney defect never show any symptoms of renal insufficiency and in my series 50 or about 12% were reported as more than 55 years old. Certain writers have placed emphasis on the connection between kidney disease in childhood and agenesia of one kidney. In my series only five under 16 years of age showed kidney disease, which indicates that there is no unusual incidence of this condition in childhood.

The four cases presented in this paper illustrate the clinical situations which face the physician in such cases. In none of them was the condition di-

TABLE I

Compiled Statistics

	Cases
Agenesia of one kidney	422
Sex stated as male	198
Sex stated as female	183
Occurring on the left side	218
Male	116
Female	87
Occurring on the right side	179
Male	82
Female	79
Remaining kidney said to be large	194
Ureter reported present on side of defect	42
Ureter reported absent on side of defect	228
Only one ureteral orifice described in bladder	104
Renal vessels reported absent	100
Associated malformations of female genitals	128
Associated malformation of male genitals	42
Adrenal absent on defective side	46
Remaining kidney misplaced	20
Remaining kidney diseased	96
Chronic nephritis	28
Stone in kidney or ureter	23
Other forms of kidney disease of serious nature	35
Kidney disease an incidental finding	10
Operative removal of single kidney	10
Other operations with death	6

agnosed clinically. In three of them the kidney deficiency had produced no clinical symptoms. One was a child, a below par individual, with other malformations, dying from diarrhoea of infancy, with an acute nephritis which was considered of minor importance as a cause of death. Another was a young girl, dying from an acute infection with septico-pyemia, the so-called malignant furuncle of the face. The third was an old woman dying of skull fracture. In the case of the old woman inflammatory foci are mentioned in the kidney, but they were of no clinical significance in her case at the time of her death from other causes. In none of these cases are there urinary findings or clinical symptoms which would in any way indicate that the one kidney existing was experiencing any difficulty in performing the work of two kidneys.

The fourth case, however, presents features of clinical interest. While in some ways a typical case of chronic nephritis, there are certain features which differ from the usual findings. The course of the disease from the earliest clinical symptoms to uremia with advanced secondary contraction of the kidney was rather short, and at no time was there the development of the usual oedema. Instead, relatively early in the disease there was an unusually high blood pressure with marked hypertrophy of the heart. In addition to this, the autopsy showed a most unusual degree of arteriosclerosis, particu-

larly in the aorta and coronary vessels. A number of cases from the literature report cardiac hypertrophy, but even in those with fairly complete clinical histories the blood pressure is practically never given, so no statement can be made as to the frequency of this finding. At the time of the patient's admission the kidneys failed to eliminate any dye, the concentration power was practically nothing, and the non-protein nitrogen of the blood was high and rapidly increasing. These findings indicate that, as might be expected, in cases where one kidney is congenitally absent, the other is not only more subject to disease, but that disease of the kidney when present tends to run a more fulminating course. While the danger of drawing conclusions from an isolated case is freely admitted, it appears that the prognosis in kidney disease is more grave in cases where there is only one kidney present.

The clinical diagnosis of a unilateral absence of the kidney is not a simple matter, and there is at present no way in which one can determine whether the condition is a true absence or a case of non-function of one kidney, except by an exploratory operation. Winter (6) after his experience in removing a single kidney recommended that in all cases where it was impossible to determine by other means the presence of two kidneys, an exploratory incision should be made over the other kidney before operating on a diseased kidney. Cystoscopy will in many cases reveal the presence or absence of the second kidney, but the mere finding of two ureteral orifices is not sufficient as in many of the cases the ureter on the deficient side persists. If the urine can be seen coming from the openings the presence of both kidneys is indicated but the degree of function on the two sides can be determined only by ureteral catheterization and dye injection. The association of any genital defect if known should place the physician on his guard for the absence of one kidney, particularly if the defect is of the type described as being frequently associated with this malformation.

The chief clinical importance of this condition lies then in the fact that the single kidney present is more subject to disease, and that disease of that kidney is more difficult to treat. At the present time, most of these cases occur as "autopsy surprises." There should be a higher accuracy of diagnosis, and this is possible only when physicians bear in mind that every case of kidney disease may be one of a congenital unilateral kidney. Having diagnosed the condition, the physician should recommend surgical operations only when absolutely necessary. Often such an individual will come in with anuria, and in such a case something obviously must be done, but the operation undertaken should be the most conservative possible. Any patient coming in with a suddenly developing anuria, particularly if associated with renal colic should awaken a suspicion of this condition on account of the frequency of stone in a single kidney, and there is considerable importance attaching to a recognition before treatment is instituted.

Summary

(1) Agenesia or total absence and aplasia, or failure of functional development, occurring in one kidney, while

rare, is a condition which may occur in any physician's practice. The computed frequency from a large series of reported instances is one case in 1290 autopsies.

(2) A series of 419 cases of agenesia of one kidney have been collected from the literature. In addition to these three new cases of agenesia and one case of aplasia have been reported, together with the clinical findings.

(3) The defect occurs somewhat more frequently in the male than in the female, but there is not the marked male preponderance reported by many writers. In males the left side is more frequently affected in the ratio of 3 to 2 while in the female the occurrence is practically equal on the two sides.

(4) Genital malformations are associated with agenesia of the kidney in 70% of the females, the most common being those due to imperfect development of the Müllerian ducts—atresia of the vagina, septate vagina, septate uterus, didelphic uterus, bicornuate uterus, and unicornuate uterus. The side of the kidney defect shows a more rudimentary condition than the opposite side. In the male genital malformations were present in 22% of the cases, the most common being an absence on the affected side of the Wolffian duct derivatives—the ejaculatory duct, seminal vesicle, vas deferens, and the tail and part of the body of the epididymis. The genital glands are rarely seriously involved.

(5) The ureter was reported as absent on the affected side in 54% of the cases and present in 10% of the cases. The renal vessels were reported as absent on the side of the kidney defect in 23.7% of the cases. The corresponding adrenal was absent in 10% of the cases.

(6) The existing kidney in a case of unilateral agenesia is more subject to disease than when two kidneys are present, kidney disease being noted in 22.6% of the reported cases as against 15% in an average run of autopsies.

(7) Surgical operations on a unilateral kidney are apt to be followed by anuria and death, and when undertaken should be as conservative as possible.

(8) Kidney disease offers a poorer prognosis in the case of unilateral kidney than when two kidneys are present.

(9) Congenital absence of one kidney is at present seldom diagnosed clinically. Its recognition depends upon a realization by the clinician of the possibility of its presence and a search for evidence of the condition, since it usually presents no clinical symptoms pointing directly to its existence.

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The Embryohormonic Relations of the Thyroid Gland to Ectodermal Tissues

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THE correlation of function among the endocrine glands has been a trying problem; but recent work is paving the way to a better understanding. Naturally, the teaching of this subject has been difficult and the student has been confused because he has no mental splint by which he can fix a systematic scheme for their study. In these articles I will endeavor to show how the subject may be made easier through the medium of embryological origin of tissues, and if this is done, the symptomatology of various endocrinopathies is more easily understood.

During a course of thirteen years, confidence in this scheme of viewing the endocrine relationship has become greater as individual portions of it have been proved experimentally.

The basis of my plan for correlating the endocrine glands rests upon the selectivity of each secretion on particular tissues according to their embryological origin.

Impetus has been given to the study of endocrinology by observations on the human constitution. Our knowledge of the endocrines makes it natural to link this study of the constitution with the specific influence of the ductless glands on the body make up.

A well known example of this specific influence is that of the pituitary gland on bone development. Another is that of the thyroid on brain development and function. That manifestations of racial body characteristics and morphology are influenced by the endocrine glands is too well known to need further emphasis. Bauer (1) especially has emphasized the constitutional study of disease; and no textbook on the endocrines is now complete without a chapter devoted to this phase of the subject.

As constitutional inheritance is studied, the impression is gained that certain groups of cells have inherent characteristics and react in specific ways to bodily (i.e. chemical) influences. It is this point that I wish to emphasize in order to provide an understanding of the selective action of the endocrine glands, disturbances of which may produce at times, anomalies such as cretins, dwarfs, giants, etc.

It is obvious that constitutional inheritance predisposes the individual to certain diseases and it is equally obvious that in a specific case certain tissues manifest this tendency.

There are many clinical examples of the selective action of the ductless glands on certain tissues. The func-

tional and genetic relationship of the suprarenal cortex to the sexual glands, the selectivity of the suprarenal medulla secretion on the sympathetic nervous system are two examples.

We are familiar with the fact that endocrine diseases produce a variable picture in different individuals. Hyperthyroidism for instance, of the same degree of severity in two individuals manifests itself in certain tissues with a varying degree of severity. This can only be understood by constitutional inheritance. The so-called local "gen" with its constitutional inheritance determines the predominant symptomatology.

Discussing with others the embryological correlation of the endocrine glands through selective action, I find that the main difficulty in understanding the hypothesis is that the impression is gained that the endocrine gland in question has a selective action on the tissues from which it originates. For instance it is thought that the pituitary, being ectodermal in origin has a selective action on ectodermal tissues. This is not necessarily true.

In studying the selective action of certain of the endocrine glands, the thyroid will be considered first, the pituitary second and the suprarenal cortex, third. It is possible that later the other glands will be considered but for the present, in order to lay a foundation, just those above mentioned will be studied.

THE THYROID GLAND.

The Thyroid has a Selective Action on Ectodermal Tissues.

The thyroid gland is developed from the entodermal layer, but has a selective action on ectodermal tissues. These tissues are:

Skin
Hair
Nails
Sebaceous and sudorific glands
Mammary gland
Eye
Auditory organ
Central nervous system
Sympathetic nervous system
Suprarenal medulla
Olfactory organ
Enamel of teeth
Pituitary gland

According to the hypothesis the function of the thyroid gland is reflected in these ectodermal tissues.

Taking as an example hypofunction, severe myxedema or cretinism, the changes and symptoms in these tissues by this disease will be mentioned.

Skin. The sebaceous and sudorific glands are derived from the ectoderm and thyroid hypofunction produces a lessened *sebaceous* and *sudorific gland* function. It is not surprising therefore that we encounter many skin changes in hypothyroidism. Cutaneous dryness is frequent. The sudorific action of pilocarpin is lessened or entirely absent. (Falta) (2). The *hair* is very dry and hypothyroid baldness is not uncommon. The sparseness of the hair is not entirely confined to the head but the axillary hair, trunk, thighs etc., are also involved. The *nails* are striated, brittle and atrophic. Janney and Henderson (3) state that at least eighty per cent of hypothyroid individuals have nail involvement. The softness of the nails produces a sensitive-

ness which is very troublesome. Scleroderma, psoriasis, icthyosis, etc., are very frequently seen in hypothyroidism. It is surprising how frequently psoriasis, eczema, and dermatitis of various sorts will give the first clue to the presence of hypothyroidism. Recently I noted the incidence of goiter with psoriasis and the number is remarkably high. That great benefit is derived from thyroid medication in many skin diseases is well known to dermatologists. That scleroderma may follow hypothyroidism as the result of thyroidectomy is well known. Why is it that only a few have this disease as a result of hypothyroidism? The explanation can be found in constitutional inheritance. In this case, the skin as a local gen shows an inherent constitutional weakness, thus bearing the brunt of the hypothyroidism in the form of scleroderma. Obviously the sebaceous and sudorific glands are severely involved. This local gen weakness may of course be manifested in other ectodermal tissues and holds true for all endocrine diseases. *The mammary glands* are usually large but this is due to the large amount of fat present and not to the lacteal tissue which is poorly developed.

Eye.—The association of hypothyroidism with *eye* conditions is a very interesting study and the undoubted influence the thyroid secretion has on the eye makes the study of great importance. Hypothyroidism would theoretically result in degenerative eye changes. That this is true clinically, is well known. Athyreosis is frequently associated with agenesia or hypoplasia of the uveal tract with resulting blindness. Corneal ulcers are also not infrequent and I have seen a case of congenital cataract with corneal ulcer in association with goiter in a girl who has since developed true exophthalmic goiter. She likewise has congenital nystagmus and is feeble minded. Zentmayer (4) says that keratitis, corneal ulceration, conjunctivitis and blepharitis may be produced through thyroidectomy. Atrophy of the whole eye has been observed. (V. Szily and Poos) (5). Radical thyroidectomy results at times in marked eye disturbances of a degenerative nature. Cataract is not infrequent. Zentmayer (4) quotes Petzetakis as saying that hypothyroidism leaves the sympathetic without the normal stimulation of the thyroid, and as a consequence vagotonus results.

Auditory organ. Hypothyroidism frequently produces changes in the function of the auditory organ, both in infancy and adult life. "The epithelium of the internal ear is derived from the *ectoderm*. The epithelium of the labryinth at first is composed of a single layer of low columnar cells. At an early stage, fibers from the acoustic nerve grow between the epithelial cells in certain regions and these become modified to produce special sense organs. These end organs are the cristae ampullares in the ampullae of the semicircular canals, the maculae acusticae in the atriculus and sacculus, and the spiral organ in the cochlear duct.

Mesenchyme surrounds the labryinth and is differentiated into a fibrous membrane directly surrounding the epithelium, and into the perichondrium of the cartilage, which develops about the whole internal ear. (6) We see from this that the ear proper is

ectodermal in origin while the source of the bony labryinth surrounding the ear proper is derived from the mesoderm. To my mind this is important in determining the origin of otosclerosis, there being a question as to whether the thyroid or pituitary is responsible, but this cannot be discussed here.

The association of deafness with cretinism is very well known. Some ascribe this to cortical deafness but this does not explain the deafness that adults have who developed hypothyroidism in later life. The pathological changes found in the auditory organ in cretinism are many and diverse. Alexander (7) has reviewed the findings of many authors and the degenerative nature of the lesions reported is striking. Many photographs of the auditory organ in its finest detail are given in this thorough and extensive review.

Barlow (8) in studying the vestibular nerve function in fifteen cases of myxedema found that there was a lessened response to stimuli. I (9) have reported twenty-four cases of hypothyroidism associated with vertigo and deafness. Eighteen of these cases who were not totally deaf showed marked improvement in hearing as well as the disappearance of the vertigo upon taking thyroid extract. These individuals did not show any striking hypothyroid signs and for this reason the association had not been previously thought of.

We may safely say that degenerative changes in the auditory organ are the rule in hypothyroidism.

Central Nervous System. The influence of hypothyroidism on the central nervous system is quite familiar to everyone. The slowing of mentality so frequently a part of the myxedematous picture produces an obvious association between thyroid function and this portion of the ectoderm—the central nervous system.

The pathology of the central nervous system in hypothyroidism depends on the time when the hypothyroidism takes place and upon its severity. Naturally the greatest pathology is found in congenital conditions such as cretinism. Idiocy and feeble-mindedness are prevalent in endemic localities. Mental backwardness is manifested early in these individuals. Older children have difficulty in acquiring knowledge and have a low intelligence quotient. The memory is poor, they are slow and sluggish in their actions. Depression and melancholia is frequent. The relation of the thyroid to certain mental diseases is at present an unsettled one, but that it influences the psyche seems likely.

Non-development of the convolutions of the brain is frequent. More emphasis is being placed by pediatricians and endocrinologists on the mental symptoms of hypothyroidism. These patients do not notice objects about them and they creep, stand and walk at a later age. We have frequently encountered psychoses in goiter patients and no doubt this association is noted in many goiter clinics. Phillips (10) observed goiter in twelve per cent of patients suffering from psychoses.

We find, therefore, that hypothyroidism is associated with degenerative changes in the central nervous system and the normal function of this system must be dependent, in part at least, on normal thyroid function.

The suprarenal medulla and the sympathetic nervous system. A definite relationship exists between thyroid function, the *suprarenal* medulla, and the *sympathetic nervous system.* Emphasis must be placed on the fact that the suprarenal medulla is ectodermal in origin, in contrast to the suprarenal cortex which is mesenchymal in origin. The medullary portion as we know produces epinephrine.

Many clinical facts demonstrate the relationship between the thyroid gland and the suprarenal medulla. Theoretically it will be noted that hypothyroidism would result in a decreased function of the sympathetic nervous system and suprarenal function. So far as the function of the latter is concerned arguments are still progressing as to whether the epinephrine is given off only during emergencies or whether it is constantly given off in low concentration. At any rate, it is a well known fact that hypothyroid individuals have a greater tolerance for epinephrine than normal individuals. Certain it is that epinephrine has a definite and selective action on the sympathetic system. The literature is full of experimental and clinical proof that the sympathetic nervous system gives a lessened response in hypothyroidism. Hoskins (11) has recently stated that in the present state of our knowledge, perhaps the most plausible assumption is that epinephrine consistently and generally exerts a biphasic effect as it has been shown to do in cases of intestinal peristalsis, uterine contractions and blood vessels in muscles. Hyman and Kessel (12) in a series of articles show the close relationship between the thyroid and involuntary nervous system.

Olfactory Organ. The sense of smell is diminished in hypothyroidism. Some believe this to be central in origin and not peripheral. The importance of this relation to the selective action of thyroid on this ectodermal tissue is not very great. However, on theoretical grounds it would be the result of central and peripheral organ involvement.

Enamel of teeth. The *teeth* in hypothyroidism are notoriously carious, dentition is delayed and if hypothyroidism continues second dentition is affected.

The pituitary gland. The relationship of the thyroid to the pituitary is a most important one and as so much depends upon showing the relationship, this phase will be discussed more fully. It is well to state that according to the opinion advanced here, hypothyroidism would result in hypopituitarism and hyperthyroidism would produce hyperpituitarism. Let me emphasize, however, that as far as the pituitary is concerned, results from hypo- and hyperthyroidism are not as severe as that seen in primary pathology of the pituitary gland.

Trautman (13) has dealt at length with the influence of thyroidectomy on the pituitary. He used thirty goats in his experiments. Thyroidectomy in these animals resulted in marked alterations in all three parts of the pituitary. He concludes that there exists an inner physiological relationship between pituitary and the thyroid. He believes that the complete or partial elimination of the thyroid causes an actual patho-

logical alteration in the properties of the blood which acts in a harmful manner on the different parts of the pituitary.

The alterations are of a degenerative type, thus proving that the pituitary cannot functionate vicariously for the thyroid. Evans (14) from his work on animals, believes that pituitary function is really reduced after thyroidectomy, though the pituitary is not smaller, and indeed, undergoes a transitory enlargement. He quotes Degener to the effect that the peculiar enlargement of the anterior pituitary after thyroidectomy does not represent the assumption of vicarious function. Mammalian experiments made by Smith and Graeser and by Flower and Evans, show that hypophosectomized animals cannot grow if given thyroid but that thyroid-free animals possessing the pituitary will grow normally or better than normally if the pituitary hormone is given parenterally along with thyroid therapy. He goes on to say that in one case we convey the growth hormone directly, in the other we furnish the animals own pituitary with a material needed directly or indirectly for its normal function. He believes that the thyroid is essential for pituitary normality. This is the real cause for dwarfism in the cretin.

Hoskins and Hoskins (15) conclude from their series of experiments on frog larvae that removal of the thyroid hastens growth, causes hyperplasia of of the pituitary and prevents metamorphosis. Smith and Cheney (16) believe that the anterior lobe preparations used by Hoskins and Hoskins contained an unusual amount of iodine and displayed an altogether unique activity. From their own work they conclude that the evidence indicates that a similarity of response is not evoked by thyroid and pituitary administrations.

Allen (17) found that in normal tadpoles in which the pituitary had been ablated, that when the anterior lobe was implanted the thyroid glands were restored to almost normal size. Berblinger (18) examined the pituitary in five people with hypofunction of the thyroid dying from intercurrent disease. He found an increased number of chromophobe cells, the cells are richer in protoplasm than normally. In the syncytial cells degeneration of the nucleus was seen. In three of the five cases the pituitary was heavier than normal. He says this increase in weight is only due to the increase of chromophil cells. He does not believe that the enlargement of the pituitary after thyroidectomy is compensatory. Vallillo (19) found that the histological observations on the prehypophyseal parenchyma of goats and horses previously deprived of the thyroid showed modifications, on the whole equal in all cases. These modifications are characterized by increase of the eosinophil cells, or by their regressive alterations. The presence of new elements determines the increase in the weight of the gland. Friedman (20) says that the pituitary appears to show histological changes in Graves disease similar to those of hyperpituitarism and in myxedema to those of hypopituitarism, and that chromophilia of the anterior lobe is characteristic for Graves disease; chromophobia for myxedema.

Cooksey (21) concludes from experiments on tadpoles that feeding thy-

roid extract produces a diminution in the size of the anterior pituitary.

Janney (22) says that the pituitary regularly hypertrophies in animals following thyroidectomy, and sometimes in myxedema.

Schoneman (23) who is extensively quoted on thyroid-pituitary relationship, reported that in one hundred and twelve cases of goiter, the pituitary was atrophied in proportion to the degenerative changes found in the thyroid. Connective tissue overgrowth, hyaline degeneration, colloid formation, vascular and chromophilic hyperplasia are found.

de Coulon (24) reported microscopic hypertrophy but diminution of the glandular tissue.

According to Falta (25) in myxedema the pituitary is commonly altered. He quotes Boyce and Beadles as finding enlargement of the pituitary as did also Ponfick. Quoting another case of pituitary enlargement with colloid degeneration of the protoplasm, Falta says that in other cases there has occurred a pronounced sclerotic degeneration of the glandular pituitary, (2nd. Case of Ponfick) or cystic degeneration. (Sainton and Rothery and others). In myxedema adultorum the pituitaries present changes of a strumous character or simultaneously with these, changes of a chronic inflammatory nature. He says in italics "The goiter poison therefore works deleteriously on the hypophysis."

Rogowitch (26), Stieda (27) and Hofmeister (28) found hypertrophy of the pituitary after thyroid removal in rabbits.

Eichhorst (29) found degenerative changes in hypothyroidism.

V. Cyon (30) found strumous alterations in the pituitary of St. Bernard dogs after thyroidectomy.

Hammett (31) who has made extensive studies on endocrine gland relationships concludes as follows concerning the thyroid and pituitary relationships. "1. Thyroid deficiency conditions a consistent hypertrophy of the hypophysis in the male but not in the female. 2. The size and presumably the activity of the hypophysis is specifically related to the activity of the thyroid when this exceeds the usual limits in either direction. 3. This relationship is conditioned by gonadal incretory activity in the female but not in the male."

He tries to dispute the interpretation placed on Flowers' and Evans' work. Hammett assumes that the enlarged pituitary means increased functional activity. Such an assumption is not justified according to the clinical data and other reported experimental work. An enlarged and altered pituitary does not postulate increased function anymore than a goiter of the colloid type represents increased functional activity. Until the pathology of the pituitary is better understood hard and fast rules cannot be drawn. It would be best, it seems to me, to use the clinical data we have to determine the functional activity of the pituitary in hypo- and in hypertrophied states.

Naturally more of these findings could be quoted but this is sufficient to show the opinions held. In summarizing the changes found in the pituitary in hypothyroidism the available evidence points to a *degenerative enlargement* of the pituitary. At the present time we are not certain as to the mean-

ing of the cell changes found in the pituitary and therefore cannot definitely interpret the significance of the cell pathology. It is certain that this enlargement does not represent functional activity, as is evidenced by the small stature of cretins and infantile hypothyroid individuals. Why do we find delayed osseous development and under developed sexual glands and organs in cretins if there is hyperfunction of the pituitary in hypothyroid states? These are all signs and symptoms of hypopituitarism. The fact is that the pituitary (an ectodermal tissue) is affected by hypothyroidism in the same manner as all other ectodermal structures and as a result of this many secondary changes due to pituitary disease supervene. This will be more fully discussed in the article on the pituitary hormone.

I will but briefly review some of the many symptoms found in the ectodermal tissues in hyperthyroidism. Naturally the tissues should show evidence of hyperactivity.

I wish to again emphasize that according to the inheritance characteristics of the local gen (referring to skin, nervous system, auditory organ, etc.) the manifestations vary in different individuals, for hyperthyroidism of the same intensity measured at least according to our present day standards, does not produce the same picture in every individual. It is a well known fact that certain systems suffer more than others which can be accounted for only through inheritance liability of these systems.

Skin. Great increase in the *sebaceous* and *sudorific gland* function is present in hyperthyroidism, so that as a result the skin is soft, oily and moist. It is of a delicate texture. These individuals like winter months best. Marked erythema is present. One of the very frequent symptoms complained of by hyperthyroid patients of severe and milder types is urticaria.

Hair. Early graying of the hair is frequent. It is usually abundant and oily, although many have loss of hair.

Nails. The nails are long and tapering. I have noticed how quickly the nails grow in hyperthyroid individuals.

Mammary glands. The mammary glands are hypertrophied and the male gland has been known to secrete colostrum.

Central Nervous system. Involvement of the central nervous system in hyperthyroid states is very evident. A rapid flow of ideas, change in character, and mental condition is often an early sign of hyperthyroidism. Irritability, excitability, insomnia and restlessness are frequent symptoms. These patients are never restful, but looking for a continual change. They are impatient, super-sensitive and often cry for trivial reasons. Apprehension and anxiety are common features. Cases of neurasthenia with rapid heart action and other neuroses, are frequently due to an overlooked goiter. One wonders how many of these cases are really abortive or mild forms of hyperthyroidism with the greatest manifestation in the sympathetic nervous system and tissues affected by this system. Some of these hyperthyroid individuals can carry on great mental labor and are never satisfied until the goal is

reached. As Howard (33) says their mental condition is aptly described by the term "chorea of ideas," Moebius (34) compares the mental state to a mild alcoholic intoxication.

Suprarenal Medulla and *Sympathetic Nervous System.* That the sympathetic system is hyperactive in hyperthyroidism is well known. The irritability of the sympathetic system is shown by the vasomotor flushing, diarrhea, digestive disturbances, rapid heart action, etc. Urticaria is frequently present. Hyperthyroid patients are very sensitive to epinephrine. (Goetsch test). De Lucas (35) says that the sensitivity to epinephrine is modified in thyroid conditions and is roughly parallel to the activity of the thyroid. Hyperthyroid individuals suffer from asthma, hay fever, and other forms of sensitization diseases.

Pituitary gland. Here again is an important and interesting relationship. It goes a long way to explain many symptoms seen in thyroid disease. Theoretically hyperthyroidism would result in hyperpituitarism. Some of the facts quoted in regard to the pituitary in hypothyroidism hold good in hyperthyroidism—such as the feeding experiments of Smith and Evans.

The incidence of goiter in acromegaly is too well known clinically to need reviewing of the literature.

Davidoff (36) found a palpable or definitely enlarged thyroid in twenty-five of a hundred patients with acromegaly.

Cushing and Davidoff (37) in their recent studies conclude that the increased metabolism frequently found in acromegaly is due not to the thyroid but to the pituitary disturbance. However, a final answer cannot be given, they say, until the active principle of the anterior lobe is isolated. They cite three cases of goiter with acromegaly who had thyroidectomies,—the thyroid gland showing colloid changes. They conclude that the evidence, despite the drop in metabolism post-operatively shows that the goiters were not active. They furthermore state that it must not be forgotten that a number of cases of exophthalmic goiter have been described as coexistent with acromegaly. They tend to question the dependableness of the diagnosis. In concluding this phase of the study they say "But all told, there is nothing in the evidence so far that would contradict the possibility that primary hyperthyroidism and primary hyperpituitarism may coexist in the same patient."

In concluding the article, they say that acromegaly is often accompanied by a palpably enlarged thyroid and by symptoms suggesting thyreotoxicosis to which the increased metabolic rate has generally been ascribed and that the chromophilic cells of the anterior lobe of the pituitary body secrete a substance which not only contains the hormone of growth, but which is capable of raising the metabolic rate. Whether the hypophyseal principle under these circumstances acts as a stimulus to metabolism directly on the tissues or only through the intermediation of the thyroid, they say cannot as yet be positively stated, although there are reasons to believe that it may act independently. It is obvious that these facts if considered objectively could just as well receive the other interpretation, namely, that in the cases they quote, the

thyroid itself was basicly responsible for the condition and that the pituitary changes were concomitant.

I have two cases at present that are definitely acromegalic individuals with primary hyperthyroidism.

Hofstaetter (38) believes that some of the symptoms of exophthalmic goiter can better be explained by an injury of the pituitary than by hyperfunction of the thyroid gland. Some of these are polyuria, polydipsia, some of the trophic disturbances, disturbances in growth, fat deposition and the insomnia. I would add that the glycosuria, hypertension, lymphocytosis and headaches were due to the pituitary but I cannot see how the insomnia can be ascribed to the pituitary.

Hyperthyroidism should result in an accelerated growth in height and a premature closure of the epiphysial structures. So it is found clinically. Holmgren (39) has shown this to be true.

Ballet (40) reported a nineteen year old girl with hyperthyroidism and gigantism.

The skeleton of the youthful hyperthyroid is slender, resembling somewhat the eunochoid type and the long tapering fingers is a frequent clinical finding. It is also noted that the joints show an abnormal amount of mobility in all directions, these individuals often performing remarkable acrobatic feats through the mobility of their joints.

Anders and Jameson (41) review the relationship between the thyroid and pituitary. In one part they say that the pituitary in myxedema is anatomically a hypertrophied gland, but physiologically an atrophied one. They reviewed two hundred and fifty cases of acromegaly and of this number changes in the thyroid were mentioned in sixty-eight. They believe that their studies indicate that the hypothyroidism is more commonly associated with acromegaly than hyperthyroidism and those combined cases which manifest myxedematous features are decidedly improved as the result of the use of thyroid preparation. It is my opinion that the stage of acromegaly has also a great deal to do with this and the state of the sex glands is also of great importance. The function of these is markedly diminished in later stages of acromegaly and this is followed by lowered metabolism.

Summarizing the findings in hyperthyroidism, the available evidence points to a hyperactive pituitary.

The next article will discuss the selective action of the pituitary.

Summary

The study of the human constitution is inseparably linked with the endocrine glands.

A better understanding of glandular relationships can be had from an embryological study. Certain of the endocrine glands have a selective action on tissues depending upon their embryological origin.

The thyroid gland has a selective action on ectodermal tissues.

This embryological correlation agrees with the facts at hand and gives an easy understanding of the symptomatology and glandular interrelationship.

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The Effect of Pituitary Administration on Growing Dogs*

By W. G. Downs, Jr., *Department of Anatomy, University of Michigan.*

THE following investigations were instituted for a study of the relationship between the glands of internal secretion and the development of the dental mechanism. While the dental phase was the one of primary interest, careful records were kept of a number of other observable results. Although the findings for the effect of hypophysis on the development of the dental mechanism were negative, (Downs, 1927) some very interesting and somewhat surprising systemic results were obtained. It is these, because of this fact, which will be recorded here.

The experimental animals used were puppies with an average age of four weeks at the beginning of the experiments, none being over six weeks old. The animals were mongrels, and consequently no information was obtainable as to their genetic makeup. To as far as possible offset the untoward effects of different blood-strains, the animals were handled by litters, so that a given experimental animal and its accompanying control were of the same age and parentage. As the investigations were primarily dental in character, no regard was paid to sex.

The experiments were divided into two series. In the first series, pituitary extracts were fed (Armour & Co's dried ox-gland). In the second series, the animals were injected with the glycerin suspension of the pituitary extracts (Parke, Davis & Co.). Throughout both experiments medication was administered at regular intervals, each animal in both series was given one dram of cod-liver oil (Mead-Johnson & Co.'s) once a day to offset the possibility of rickets and all of the animals were wormed when the need for it became evident in any of them. All animals were weighed and carefully examined every five days. Daily note was made of any changes in the outward appearance or behavior of any of the animals, and both during the experiments and at the time of necropsy for all experiments, all unusual conditions noted were compared with the evidence obtained from the literature.

For the first series, five litters of four puppies each were used. In each litter one dog was fed the extract of the anterior lobe of the hypophysis, one that of the posterior lobe, one received whole-gland extract, while one, the control animal received a normal

*The experimental work involved in these investigations was pursued in large part at the Department of Anatomy of Indiana University, Bloomington, Indiana.

diet only. The dosage was computed so as to be nearly proportionate to the maximum dosage for a human of average weight. This dosage was, in the case of the anterior lobe extract, ½ grain, of the posterior lobe extract, 1/40 grain, and of the whole gland ½ grain, each 3 times a day. Beginning four weeks from the initiation of this experiment entire litters were killed at intervals of four weeks. The animal was examined for gross changes, the tissues of the mouth, the hypophyses, thyroid and parathyroid glands were studied microscopically, and the vertebrae and tibias, as representing typical short and long bones, were cleaned and studied by the silver nitrate method of Bills (1925) for variations in calcification. The tissues for microscopic examination were uniformly prepared, having been fixed in 10% formalin, imbedded in paraffin, stained with chloral hematoxylin and counter-stained with eosin.

No definite variations in size, number, form, nuclei or standing qualities of the various cellular constituents could be observed in either of the litters. This does not coincide with the results obtained by Goetsch (1916), who obtained positive results from feeding experiments. It is felt, however, that in these experiments the size of dosage used and the period over which the experiments were conducted should be adequate to bring out any changes which might occur in such animals as dogs by glandular medication per os. The examination of the bones likewise yielded entirely negative results. There was, furthermore, no typical variation in temperament, behavior, hair color or texture which might not be expected of animals of such uncertain genetic origin. It is felt that the findings from the experiments in feeding the pituitary extracts, as regards bony growth, general metabolic changes, and changes in the gland itself, were entirely negative.

Such was not, however, the case with the second series. These were injection experiments. As has been noted the type of animals used, methods of handling, proportionate dosage, and methods of examination were identical with those used in the first series. For these investigations six litters of three puppies each were used. In each litter, for the first six weeks, one dog was injected with three minims of antuitrin (Parke, Davis & Co.) twice daily. One dog received three minims of pituitrin (Parke, Davis & Co.) twice daily. One dog, the control animal, received three minims of sterile water twice daily to offset any possible differences due to the traumatic effect of the injections. After six weeks of this dosage, although no marked untoward systemic effects had been noted, it was felt that the dosage was disproportionately large, and the dosage was reduced to one minim in each case, twice daily.

At the beginning it was intended that these animals be killed and necropsied at the same intervals as those in the preceding series. On the twenty-eighth day one litter was killed and on the fifty-sixth the next. At about the sixtieth day a number of the remaining animals began to develop symptoms of worms. All of the animals were wormed thoroughly. After the worming, the control animals and those receiving the posterior lobe extract ap-

peared to recover quickly, but the animal receiving the anterior lobe extract in each of the remaining four litters seemed unable to overcome the results of the parasitic invasion. On the sixty-fifth day, because of the extremely weakened condition of the animal receiving the anterior lobe extract, it became necessary to kill another entire litter. On the eighty-third day, the animals being injected with anterior lobe extract of two more litters were in such a bad condition that both entire litters were killed and examined. Just subsequent to this the three remaining animals developed spasms—apparently worm fits, and it was felt necessary in spite of the weakened condition of the animal receiving anterior lobe extract, to worm them. On the ninety-ninth day, the animal being injected with the extract of the anterior lobe, of the last litter died and thus terminated the experimentation.

The results obtained in the second series of experiments were practically constant for the dogs receiving the same type of medication. In weight gain, for the first eight weeks, there was very little regular variation in the weight curves. Beginning about this time a constant variation began to be perceptible. While the curves for the control animals of the remaining litters remained a practically straight line, there began to be a slight rise in the curves for the animals receiving posterior lobe injections, with a coincident marked and constant decrease in the curves for those receiving anterior lobe extract. So regular were these variations within the different litters, that the curves for either litter would almost be descriptive of those for any other litter. (See fig. 1.) A remarkable feature of the weight changes of the different animals is the contrast between the regularity of occurrence in the injection experiments, and the complete lack of regularity in the feeding experiments.

In the injection experiments some decided changes in external characteristics were likewise noted. While there was no noticeable difference in the external genitalia, as remarked by Cushing (1912), Goetsch (1916) and Beck (1912), there were differences in other external appearances coinciding in large part with their findings. The animals on anterior lobe extract had longer, coarser, drier coats. While they were, on the whole, more somnolent, they were at the same time bad-tempered when aroused, hyperesthetic to pain stimuli, and in the later stages they developed frequent and progressively pronounced epileptiform seizures. On the other hand, the animals on posterior lobe medication had a shorter, softer coat, were more active, less sensitive to pain, were even-tempered and affectionate, and their tapeworm fits were considerably lighter than even those of the control animals. These findings are almost directly opposite to those reported by Goetsch. The animals receiving anterior lobe medication showed a marked diuresis for a short time after injection, while if a variation in the frequency of micturation or the volume of urinary output was present in the other animals, it was not great enough to attract attention. This is not greatly at variance with the findings of Hammett, who observed that when the posterior lobe extract was administered subcutane-

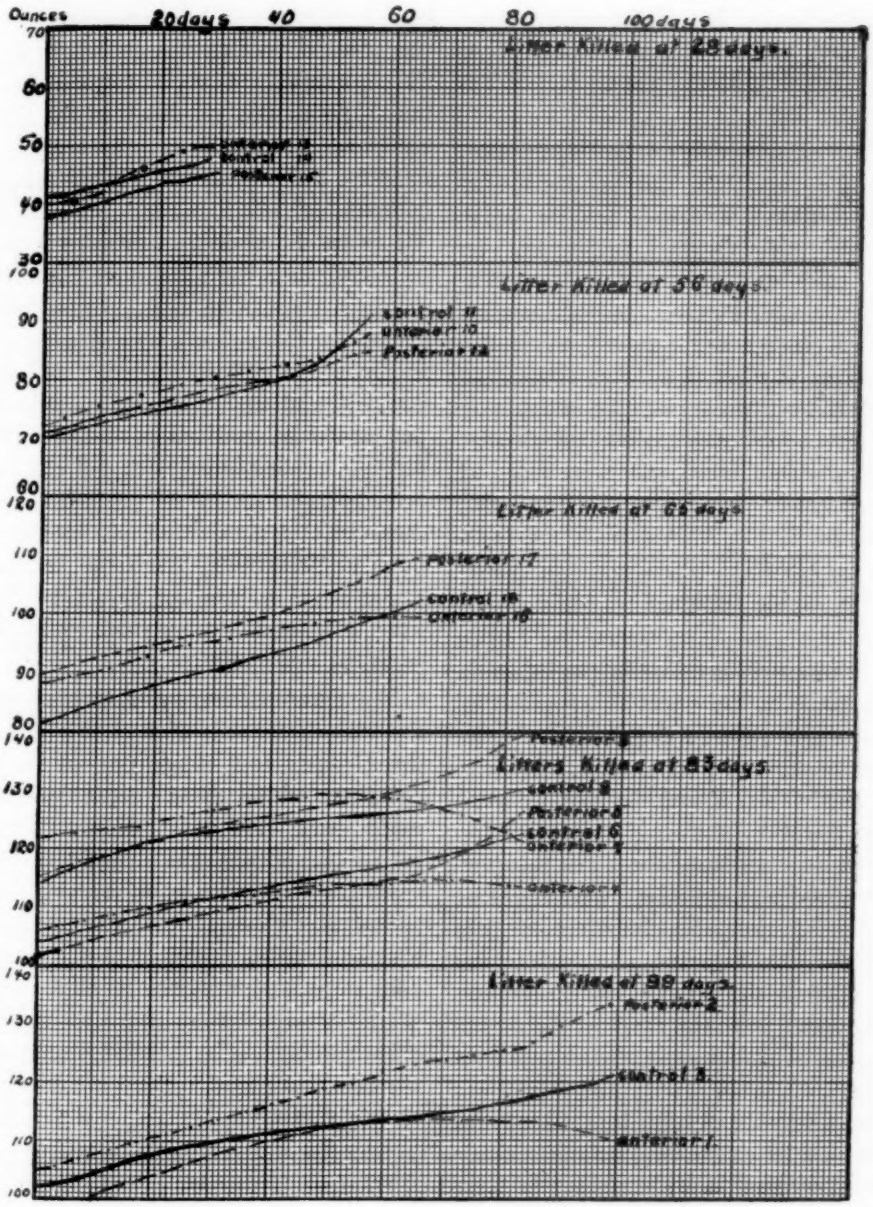
Ounces
20days
40
60
80
100days
Litter Killed at 28 days.
Litter Killed at 56 days.
Litter Killed at 65 days.
Litters Killed at 83days.
Litter Killed at 99 days.
control 2
anterior 1.

FIG. 1

ously it was apt to have an antidiuretic effect. It does, however, disagree with the findings of Motzfeldt (1917) who obtained an anti-diuretic effect from the administration of the extract of the anterior lobe.

The examination of the short bones, i.e., the vertebrae, was productive of only negative findings, but the tibias yielded some marked variations. In the case of the animals receiving anterior lobe extracts, the tibias were notably larger and showed greatly delayed epiphyseal closure as contrasted with the controls, while the animals on posterior lobe medication had smaller tibias, with a more advanced stage of calcification. This, again, is in decided contrast to the results from the feeding experiments, where no regular differences could be noted.

It has been noted during the course of the experiment that in the injection experiments, there was an apparent increase in height in the animals receiving the anterior lobe extract. In order to check this, it was decided to work out a ratio between long bone and short bone development. For this purpose, two measurements were made of each dog, immediately after he was killed. One measurement, which was designated the short-bone component, was taken from the crest on the medial border of the scapula to the posterior superior iliac spine when the animal was laid on its side with the legs extended at right angles to the long axis of the vertebral column. This became, then, a coefficient for the size of the more constant short bones, the vertebrae. The other, or long bone component, was measured from the sole of the pad of the forefoot to the eminence on the medial border of the scapula, while the animal was in the same position. For each animal the length component was then divided by that for the height and the ensuing figure carried to three decimals. With this resultant as the first component and 1000 (representing the height), as the second, a constantly comparable ratio resulted. (See Table I). From the table thus evolved it will be noted that the long bone development is constantly and progressively greater in the animals receiving anterior lobe extract, intermediate in the controls, and smaller in the animals on posterior lobe medication. This would seem to be in accord with the current views on the causes of gigantism and dwarfism. Again, it is in decided contrast to the results from the feeding experiments where no regular variations in height as opposed to length could be demonstrated.

The examination of the glands from the various animals elicited only minor differences, and those not of fixed character within the different types of medication. The gross examination of all of the glands was negative. The microscopic examination showed no mensurable change in the size, number, arrangement or nuclei of the secreting cells or colloid material of either lobe of the hypophysis or of the thyroid or parathyroids. The gonads, pancreas, thymus and pineal were not examined microscopically.

Bandler (1920) believed that the difference in growth and development in the respective sexes was largely due to the effect of the sex glands on the pituitary. An increase in the secretion of the anterior lobe in either sex caused a large bony growth, coarser

TABLE I

Animal	L-component		H-component	Time killed
No. 10 (anterior)	880	to	1000	56 days
No. 11 (control)	820	to	1000	56 days
No. 12 (posterior)	875	to	1000	56 days
*	*	*	* *	*
No. 13 (anterior)				
No. 14 (control)	No examination of bones made on this litter.			
No. 15 (posterior)				
*	*	*	* *	*
No. 16 (anterior)	880	to	1000	65 days
No. 18 (control)	870	to	1000	65 days
No. 17 (posterior)	820	to	1000	65 days
*	*	*	* *	*
No. 4 (anterior)	890	to	1000	83 days
No. 6 (control)	870	to	1000	83 days
No. 5 (posterior)	820	to	1000	83 days
*	*	*	* *	*
No. 7 (anterior)	895	to	1000	83 days
No. 8 (control)	870	to	1000	83 days
No. 8 (posterior)	825	to	1000	83 days
*	*	*	* *	*
No. 1 (anterior)	895	to	1000	99 days
No. 3 (control)	875	to	1000	99 days
No. 2 (posterior)	825	to	1000	99 days

and heavier hair and the development of the masculine type of secondary sex characteristics. His investigations revealed the exactly opposite effect from an increase in secretion of the posterior lobe. He believes that marked hypersecretion of the posterior lobe causes acromegaly, as well as an abnormal accumulation of fat, particularly shoulder and girdle deposits. These findings agree in large part with those of Englebach and Tierney (1922). My own investigations would lead to conclusions in accord with these except that it would seem that changes in the bony skeleton would follow oversecretion of the anterior rather than the posterior lobe. It is a little difficult to follow Bandler's conclusions, in that, although he attributes acromegaly to oversecretion of the posterior lobe, he at the same time finds the increase in secretion in the anterior lobe responsible for stimulation of bony growth. My own animals receiving anterior lobe extract did show a considerable increase in length and size of long bones with a coincident longer and coarser hair development. The posteriors showed almost the direct reverse.

Bandler speaks of polyuria in his animals on posterior lobe extract. Such I did not find to be the case. On the other hand in my animals receiving anterior lobe extract immediately after injection I could easily note a decided

increase in both frequency and quantity or urinary output. If there was any variation in this respect between my animals receiving the extract of the posterior lobe and the control animals it could not be noticed.

Crowe, Cushing and Homans (1910) found that repeated subcutaneous injections of the sterile extracts of posterior lobe led to emaciation. My own results tended rather to the opposite direction. I noticed a marked emaciation in the animals receiving anterior lobe injections with the opposite effect in those on posterior lobe. It is possible that a somewhat larger dosage may have so stimulated metabolic processes in my animals that the end result was emaciation. It is likewise possible that the wormy condition of my dogs was sufficiently marked to completely offset the effects of the medication.

However, in accord with P. E. Smith (1926) I am inclined to believe that the discrepancy in results so frequently noticed in endocrine experiments is probably due to the different methods of preparation used by the various manufacturers of the commercial products.

Summarizing—the feeding of pituitary preparations produced no observable changes. Injections of the posterior lobe extracts produced plumper, better proportioned and better-natured animals with soft, silky coats and an increase in epiphyseal calcification of long bones. Injection of the anterior lobe extract produced the reverse—emaciation, coarse, ragged coats, the "gigantic" type of skeletal development, bad-tempered animals, and a markedly delayed epiphyseal closure. In neither case was there a sufficiently marked change in the various endocrine glands to be susceptible of classification. The discrepancies found between this series of investigations and those of numerous other workers probably bears out P. E. Smith's claim regarding the wide variation in methods of preparation of the commercial endocrine products.

I am greatly indebted to Dr. J. A. Badertscher of the Department of Anatomy of Indiana University for his kindly advice and guidance in a major portion of the experimental work involved and to Dr. G. Carl Huber of the Department of Anatomy, University of Michigan for his oversight and criticism of the manuscript.

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The Alimentary Canal of the Medical Student, Radiographic Studies*

By T. Wingate Todd, *Cleveland, Ohio*

THE emotions which express themselves through the alimentary tract have not yet been thoroughly studied. Some slight attention was given them during the later part of the Great War when we discovered many men who had literally no stomach for fighting. Further, insufficient attention has been paid to the mechanism and appearances of the normal tract, and we need to revise the technique of our routine examinations. There is nowadays, for example, no lack of power in our X-ray apparatus causing us to demand a starved stomach and purged bowel to enable us to see through a patient.

The willing co-operation of the medical students provides us with: first a layman unused to and somewhat apprehensive of all the strange and unknown experiences to which he is to become accustomed: and secondly a medical "man" perfectly attuned to all the sounds, sights and smells which are inseparable from a medical education. Further, both these phases occur in the same individual and can therefore be directly compared. The emotions which are reflected in the alimentary tract are not conscious ones. The lack of tone in the Freshman's stomach, the stagnation in his duodenum, and the spasm of my own bowel the first time I underwent a long and possibly dangerous X-ray exposure cannot be influenced by any control on the part of the individual.

The movements of stomach and bowels may or may not be directly related to the passage onward of the contents which "seep" along whether peristalsis be present or not. In the small bowel the peristaltic wave changes its speed under different circumstances and is exceedingly slow in that part of the small bowel near its opening into the large bowel when the latter is spastic. The large bowel, contrary to what most of us have thought, presents precisely the same peristaltic wave as the stomach but with only half the speed of the stomachic peristalsis.

Apparently the stomach must be filled to a certain amount before it will empty even if vigorous peristalsis is present. The student stomach practically empties within 1½ to 2 hours. It will rapidly lose tone and possibly fill with gastric juice by the mere suggestion of food.

*Abstract of address presented to the College of Physicians, Cleveland, Ohio, February, 1927.

Summary

1. The study of the normal alimentary tract in health of young male students affords a criterion for observation of pathological conditions.

2. All parts of the tract are exceedingly sensitive to emotional or nervous conditions. These influence different parts of the tract in divers directions. The stomach becomes atonic in outline though not in movement or in emptying time. The duodenum shows pseudostasis. The transverse colon exhibits a spasm which may absolutely inhibit the onward passage of contents.

3. The sites of cardia and pylorus are affected in similar manner though not so greatly as are the positions of the greater curvature in the pyloric vestibule and gastric tube.

4. The normal position of the small intestine in the living, whether upright or horizontal, is in the lower abdomen and true pelvis: its disposition is in ladder coils.

5. Peristalsis in the lower ileum may be exceedingly slow in spasm of the transverse colon, one wave taking half an hour to complete its cycle.

6. The proximal colon (caecum, ascending colon, transverse colon) exhibits a peristaltic wave like those of the stomach and small intestine. Its rate of progress in the transverse colon is about half that of stomachic peristalsis.

Transfusion in Preoperative and Post Operative Conditions With Anemia

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IMPROVED methods of Blood Transfusion within the past 10 or 15 years accompanied by a more thorough knowledge of blood grouping and cross-agglutination tests have made the transfusion of blood a considerably safer procedure than it was previously. Former hazards, such as sudden death and reactions of various types including chills, nausea and vomiting, high fever, etc., have been reduced to a minimum so that fear of these does not contraindicate the procedure in any way. The first transfusion upon a human being appears to have been done in France by Jean Denys of Montpelier, physician to Louis XIV on July 15, 1667. Richard Lower and a group of English experimenters had been performing transfusions on animals previous to this time and were waiting a suitable opportunity to transfuse a human being. Owing to the bad results obtained by using animal blood in human beings the procedure was abandoned for over a hundred years. In England, James Blundell, the obstetrician, reported a successful transfusion of a patient with human blood in 1824 using a special syringe he devised for this purpose. His prophecy made then that transfusion by the syringe is a very feasable and useful operation and after undergoing the usual ordeal of neglect, opposition and ridicule will be admitted into practice—should place him in our memory for the accuracy of his prophecy.

The method of choice in the series of cases reported in this paper is the Lindeman direct syringe method. Blood grouping has been done merely for the sake of finding donors of the same group or of a universal group either by Brem or Moss classification to be cross agglutinated with the recipient's serum and corpuscles. At no time has a donor been chosen from a universal group or of the same group and used without first being cross agglutinated both as to cells and serum of each. Also, if the slightest agglutination is observed in either of the cross agglutination tests done microscopically, the blood has not been used. By safeguarding one's self by careful cross agglutination tests one need not fear serious results. Other safeguards such as cross agglutinating the blood after one transfusion before choosing a donor for a second transfusion on the same recipient; not using the same donor on the same recipient the second time; and careful inquiry into any history of allergic phenomena, prevent reactions to a considerable degree. In only one instance have I used the same

donor the second time, on the same recipient and this was in a case of extreme emergency where the patient's brother had to be used because of lack of time in which to find another donor. This case will be discussed later in this paper.

Owing to the fact that various subgroups of blood exist and also that people of the same group or of a universal group cause marked agglutination to appear in the cross matching of the bloods it is very unwise and disastrous at times to depend upon grouping alone unless the emergency is such, as it undoubtedly is in some cases, to warrant the use of a universal donor or donor of the same group. The natural cause of death is better explained than one following any mechanical procedure.

In all cases transfused within the past six years it has been the policy to introduce ten c.c. of blood into the vein of the donor and then wait for two or three minutes before proceeding. An accurate check of the pulse at the beginning and at the end of this time is taken. If the patient complains of any type of peculiar feeling or the pulse is raised very much, a longer period of time is taken before proceeding. The Lindeman multiple syringe and canula method has a distinct advantage in this respect since the transfusion may be stopped or started at will without fear of changing the blood to be given or having the experience of any clotting in or sticking of the apparatus.

Only in a very few instances have two donors been used on the same recipient at one transfusion. It is best to use but one donor and repeat the transfusion if necessary at some later hour and then only after a careful cross matching of the bloods of donor against donor and donors against recipient has been done. By taking the time to perform these simple tests one may save the patient a disastrous result or a severe reaction which in itself is extremely unpleasant to both the patient and the operator.

The gradual loss of blood over a period of weeks, months, or years, reducing an individual to an anemic condition, weakness and ill feeling does not cause the serious results that the sudden loss of blood produces. Gradual loss of blood may have serious end results, still the patient has a better opportunity to adjust himself to the condition, than in the case of sudden loss of blood in large quantites. Sudden loss produces shock to such a degree that death may occur very rapidly because of the sudden collapse in the heart and blood vessels. Volume of blood is the important factor, and when reduced almost instantly, as in some cases, does not allow sufficient time for adjustment to the condition. Some of the volume can be replaced by intravenous saline or glucose, but both of these solutions are lost very rapidly, and neither has the properties to increase clotting time and thereby stop bleeding at the point where hemorrhage is taking place. After a patient bleeds to a certain stage, he seems to lose all properties of clotting. Whole blood seems to fulfill the need of shortening clotting time, building up volume, and all around adjustment of the blood system better than any other substance used to date. Results are almost magical as well as extremely

gratifying in the great majority of extreme and severe hemorrhage cases if done early enough.

Some physicians believe that hemorrhage will be increased if a transfusion is resorted to, to build up blood volume immediately after loss, but such is not the case in my series of cases. Blood when given shortens the clotting time instantly as has been proven in operative procedures where transfusion has immediately preceded the operation. A small amount of blood allowed to run into a small gall bladder spoon permitted of the same being inverted in two to two and one-half minutes with complete clotting whereas blood taken before transfusion would not clot to this extent in twelve to eighteen minutes. It has also been shown that very low blood pressure is not materially raised, especially in the presence of large blood loss and the shortening of the coagulation time that results is greatly to be desired. Cases with marked jaundice in which longer than normal clotting time is practically always present have been prepared for operation by giving a small transfusion beforehand and the method of testing clotting time as mentioned with a small gall stone spoon has been used to determine this factor before and during operation. The clotting time is unquestionably shortened after transfusion.

A very interesting feature observed in a large number of cases transfused where the loss of blood has been quite profuse—is the pulse rate. This deserves mentioning because of the fact that the writer has observed a pulse rate of 172 reduced to 116 in eight minutes after starting a transfusion of 900 c.c. of blood. In practically all cases where a very rapid pulse has been encountered the rate has been reduced very markedly. Later the pulse may rise again slightly if enough blood is not given to reproduce a fair blood volume, but usually keeps on decreasing to within normal limits if the original cause of hemorrhage does not play too important a factor.

Reducing reactions of any consequence to a small percentage, in cases in which the surgeon has to carry out a mechanical procedure immediately following the transfusion certainly allows him a better opportunity to do his work more carefully, thoroughly, and with far less danger to the patient. I believe that more anemic patients should be transfused before an operative procedure is resorted to, especially in acute hemorrhage cases and in cases of chronic sepsis of the type that produces secondary anemia of a marked degree, or chronic cases of bleeding from various surfaces such as the bladder, kidneys, and intestinal tract. Certainly, the surgeon should consider a transfusion as a great aid in these cases if his operative mortality will be reduced. If the patient is built back to within normal limits of blood volume he can better undergo the more serious types of operation.

The term, "Reactions of no consequence", is used in this series of cases to mean that a slight elevation of temperature of 99 to 101 degrees, such as would be encountered in almost any operative procedure, or a feeling of malaise for several hours does not constitute a reaction in the strict sense. Cases in which chills have been produced with pains in the back, down the

legs, severe headache, and sometimes nausea or vomiting accompanied by a marked rise in temperature illustrate a reaction of consequence. If the surgeon who is to operate the case after transfusion can be convinced that a reaction will not take place in more than one out of ten to twenty cases, surely he realizes his chances of relieving certain conditions, where excessive bleeding has taken place, are better if operated on at once than if he allowed the patient to start bleeding again some little time after the transfusion. In other words he can operate immediately after the transfusion.

The preoperative sudden hemorrhage conditions with which this paper deals are ruptured ectopic pregnancy, hemorrhage from a gastric or duodenal ulcer, severe hemorrhage in miscarriages or septic abortions, perforation of intestine (caused by accidental trauma to abdomen), ruptured spleen, hydatid mole and varices of esophagus from cirrhosis of liver. The preoperative gradual hemorrhage cases are ulcerative colitis, hemorrhage from uterus due to fibroids, polyps and endometritis, following abortion or miscarriage and Hunner ulcer of the bladder.

Postoperative sudden hemorrhage conditions are: uncontrolled hemorrhage following tonsillectomy, post partum hemorrhage, hemorrhage following gastroenterostomy, placental detachment in utero-prepartum and ruptured uterus during curettment. Postoperative conditions with gradual loss of blood which were transfused were: secondary anemia following empyema and rib resection, mastoiditis, miscarriages, and cases of osteomyelitis. Several cases of some of each of the above named have been transfused but for the sake of brevity but one case of the more marked conditions will be given in this series.

Case I. Female, age 27. Intra-abdominal hemorrhage from ectopic pregnancy. When first seen by surgeon on Oct. 24, '26, patient was in a state of collapse and complaining of numb feeling all over her body as well as extreme weakness. Marked air hunger. Pulse 162, R. B. C 1,780,000, W. B. C. 13,400, and hemoglobin 35%. 700 c.c. of blood given, pulse reduced to 108. Color of patient considerably improved at time of transfusion. Surgeon waited for two hours to see if any reaction would take place. There was no rise in temperature or chill. Abdomen opened. Ruptured ectopic pregnancy found and removed. Patient made uneventful recovery and left the hospital on the 12th day. Highest temperature posttransfusional and postoperative was 102.4 degrees.

Case II. Female, age 61. Seen November 18, 1922 at 12:30 a. m. About one-half hour before seeing patient she began vomiting bright red blood and passing blood in her stools. She was in complete shock. R. B. C. 1,220,000, W. B. C. 16,800, and hemoglobin 30%. She was sent to the hospital and transfused, 600 c.c. of blood given. Transfusion repeated in eight hours. Pulse reduced from 174 to 120. Abdomen opened. Ulcer excised by cauterization method. Made uneventful recovery. No reaction from transfusion. Highest temperature after operation and transfusion was 102.8 degrees.

Case III. Female, age 31. Ambulance case to the hospital March 14, 1921. Had abortion performed two weeks previous to admission. Bleeding from uterus constantly and very profusely for two days. Pulse not obtainable at wrist. Pulse over heart 166. Extremely pale and ashen in color. R. B. C. 1,180,000 and hemoglobin 30%. Intravenous saline containing one-half c.c. adrenalin given. Chill following this. Blood trans-

fusion 1,200 c.c. given using two donors. Temperature on admission 103.6 degrees. No reaction from transfusion. Uterus emptied immediately after transfusion. Uneventful recovery.

Case IV. Male, age 27. Brought into hospital April 7, 1921, following automobile accident. Was in state of collapse. Diagnosis made of perforated intestine with severe hemorrhage into abdomen. Blood transfusion, 920 c.c. blood given. Pulse reduced from 162 to 130. Perforation of intestine found with large amount of blood in abdominal cavity. Temperature following operation and transfusion was 102.6 degrees. Three days later wound broke wide open. Sutured. One week later patient began having severe pain in left side of abdomen with marked increase in pulse and temperature. Abdomen opened and volvulus found. Patient developed ether pneumonia following operation. Another transfusion of 640 c.c. was given because of his anemic condition at this time. Had rise of temperature to 104.8 degrees with slight chill. Went on to complete recovery in three weeks.

Case V. Female, age 7. Seen March 6, 1921. While coasting on a sled she ran into a park bench, left side of body striking bench with considerable force. Patient in shock. Abdomen distended. Blood transfusion 560 c.c. of blood given. No reaction. Operated one hour after and ruptured spleen removed. Highest temperature after transfusion and operation 103.4 degrees. Uneventful recovery.

Case VI. Female, age 26. Seen July 15, 1925. Had been bleeding profusely from uterus for three days. Condition fair, Pulse 144. R. B. C. 2,120,000, and hemoglobin 45%. Transfused, 650 c.c. of blood given. Pulse reduced to 110. Two and one-half hours after transfusion hysterectomy was done. This case proved to be a hydatid mole. Highest temperature 102.6 degrees. No reaction from transfusion.

Case VII. Male, 25 years of age. First seen in hospital April 1, 1921. Vomiting large quantites of blood bright red and dark. In state of collapse and very pale. 580 c.c. of blood given. No reaction. Six and one-half hours later 710 c.c. of blood given. Had chill lasting 20 minutes following second transfusion. On following morning abdomen was explored and cirrhosis of liver found. Omentopexy was done. Patient recovered sufficiently in one month to leave the hospital in fair condition.

Case VIII. Female, age 25. First observed October 12, 1926. Bleeding from uterus constantly for one and one-half years. R. B. C. 2,120,000 and hemoglobin 40%. Transfusion 510 c.c. Bleeding did not stop entirely although decreased. Transfused again January 1, 1927, 600 c.c. of blood given. No reaction. Highest temperature 99.6 degrees. On following day D. & C. was done by surgeon. Radium used in uterus. Patient in good condition to date.

Case IX. Male, age 65. First seen February 20, 1927. Bleeding from bladder off and on for past fifteen years. Practically constantly for past three months. Hemoglobin 24%. The surgeon after cystoscopy made diagnosis of Hunner ulcer of bladder. Transfusion 690 c.c. of blood given. No reaction. Highest temperature 100.4 degrees following this. On March 1, 1927 620 c.c. of blood was given. No reaction. Temperature 100.2 degrees. Operated March 8. Patient in excellent condition to present time.

Case X. Female, age 31. Seen February 21, 1925. Following tonsillectomy had severe hemorrhage from throat during the day. Was given salt solution in large quantities without result. At 8:00 p. m. she became unconscious and pulseless. 580 c.c of blood given one hour after this with result that patient became conscious with the finishing of transfusion. No reaction. On July 19, 1926 at eight and one-half months pregnancy this patient had a detached placenta in utero with marked evidence of severe hemorrhage. Surgeon performed caesarean section and upon finishing operation patient was transfused 560 c.c. of blood be-

ing given. Due to extreme emergency the same donor (her brother) was used in this case as on the first transfusion, one year and four months previously. Patient at this time had chill lasting about twenty-five minutes. No marked febrile reaction with this. Highest temperature being 102.8 degrees. She went on to complete recovery.

Patients with hemoglobin of 20 or below have been known to be successfully operated upon as shown by Baldwin. Lahey in his recent article on preoperative preparation of patients states that "No longer may one defend his position when operating on a poor risk, anemic patient, who has not had a blood transfusion previous to operation." The trend of the busy surgeon today is to realize this fact in its strictest sense because he knows from past experience that his mortality is unquestionably decreased in severe hemorrhage cases if transfusion is done previous to or immediately following his operative procedure. Also in secondary anemias of a more or less chronic nature as in some of the cases illustrated the patient has been made a good operative risk by transfusion.

Stoll in his recent article reports 100 cases done by his modification of the Lindeman method in which he works alone in doing the transfusion with a reaction in eight out of 100 cases. Last summer I had the opportunity of timing him while transfusing by this method and the shortest time that the blood was out of the body was one and one-fourth minutes and the longest time one and three-fourths minutes. The average length of time in the Lindeman method should not be more than 12 to 18 seconds from the time that the blood is started into the syringe until it has been entirely introduced into the recipient's vein.

In shock it is now generally believed that the symptoms are due to a universal capillary dilatation which results in so much of the blood remaining in the capillary beds that the return flow to the heart is not adequate and the arterial blood pressure becomes very low. Apparently the individual bleeds into the capillary beds and not into his veins as was formerly thought. As a result the tissues suffer from lack of oxygen, which in turn leads to still further dilatation of the capillaries and in the more advanced stages to increased permeability of the vessel walls, so that a loss of plasma occurs, thus aggravating the circulatory failure. Transfusion if performed early restores the circulation and corrects the serious oxygen lack to the tissues. It is not of much value when shock has existed for several hours and the patient is practically moribund. If a lengthy and serious operation is to be performed in which shock is likely to take place it would be advisable to have the bloods cross agglutinated beforehand in order to lose the least time possible in performing the transfusion.

The contraindications of transfusion preoperative or postoperative are but very few—being acute cardiac conditions such as fresh vegetations on the heart valves or acute cardiac dilatation and certainly if surgery were indicated with these complications it would have to be postponed anyhow.

Summary

Careful checking of the recipient's blood with that of the donor is absolutely essential for safety. The blood

should always be re-cross agglutinated after each transfusion if another is to be done. Consequential reactions of the type described which occur in approximately five to ten percent of the cases should not be a contraindication for transfusion.

The indications and limitations for preoperative and postoperative transfusions should be better understood and advantage taken of the same more often.

Transfusion is the most successful means of combating severe hemorrhage or shock yet devised both preoperative and postoperative.

In chronic secondary anemic patients, transfusion undoubtedly makes the patient a better operative risk and its use may be life saving.

The Laboratory Service in Civilian Hospitals

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Part I

As indicated by the title, this paper will deal with conditions obtaining in civilian hospitals for the physically ill, where they concern the laboratory service, though much that will be said might have application to the military service and to the service of mental hospitals.

Comparing the major services of a hospital—medical, surgical and laboratory,—we find a similarity which is useful for our purposes. Each major service has its acute cases, which demand short-time, intensive attention and its subacute or chronic cases, which demand prolonged, extensive attention.

In the first type of case, the physician or the surgeon is accustomed to request this or that procedure as he is guided by the indications in the case. One can scarcely condemn this practice where an emergency is concerned or where the diagnosis is clear or where the laboratory physician is little better than a technician. But in hospitals where the laboratory is in charge of a worker with clinical sense and experience, a consultation with the laboratory service may save a mistake in diagnosis—though the diagnosis was previously clear—and no element of time may be added to complicate the existent emergency.

A case in point is indicated:

E. L., female, white, 20, school girl, was admitted with a diagnosis of acute appendicitis. The white blood count was 22,800 with 89% polys. The urine showed a trace of albumin and sugar, an occasional pus cell, three plus red cells (patient not menstruating), two plus renal tubule cells, and acetone.

Operation revealed a normal appendix and no abdominal pathology, but the right kidney was thought to be enlarged. Following operation the white blood count was still 20,000 and repeated urine examinations showed a definite acute nephritis with low volume output. Blood culture showed a gram-positive coccus and a gram-negative bacillus which were apparently of low virulence as the clinical course of the disease demonstrated.

Catheterization of the ureters revealed blood and pus from both kidneys and the left one showed bacteria in the urine. Recovery was prompt and uneventful, under treatment for the kidney condition.

A second case in point is as follows:

A. N. E., female, white, 53, housewife, was admitted with a diagnosis of orbital cellulitis. The course of the disease showed that the portal of entry was probably the throat, with extension to the nose and, later, to the orbital structures. Smear from the right

tonsil, which showed a small amount of exudate, revealed Vincent's organisms and cocci; the nares showing bacilli and cocci; the orbital exudate showed cocci. Smear and culture were negative for diphtheria. Culture from the nasal and orbital exudate showed a short-chained gram-positive coccus which was lytic for coagulated blood serum. This organism grew as a pure culture on primary incubation.

White cell count was 1200. This finding was so surprising that it was repeated at once using fresh diluting fluid; the finding was 200. To make certain of our fluid a "normal" person was taken; her count showed 12,800 (she had just had a cold bath). The patient's count was first done thirty minutes after the administration of streptococcus anti-toxin intravenously. Twelve hours later the white count was 2,600; red count 3,950,000; polys. 28%, large mononuclears 26%, small mononuclears 44%. Another intravenous injection (this time antistreptococcus serum, polyvalent) was given. Two hours later the white count was 3,000; twelve hours later it was 800 and twenty-four hours later it was 1600.

Treatment included transfusion in order to bring up the power of resistance of the body, but patient grew worse progressively. Outcome was fatal.

These two cases, one surgical and one medical, show how the laboratory can be of service in emergency cases, without increasing danger by adding to the time element involved. In one case, we had the diagnosis and treatment correctly given by the laboratory findings where the clinical signs had misled the surgeon. In the other case, the laboratory findings showed a hopeless prognosis, at the same time indicating the only known form of treatment that might offer hope of a favorable outcome.

I have selected these two cases because the usual run of routine cases with the usual laboratory findings are well known to everyone. At the same time, I want to stimulate the clinician, whether he is physician or surgeon to call in the laboratory more frequently even in his so-called "clear" cases.

Part II

The Laboratory can be of still greater service in the subacute and chronic case. It is not our intent to exalt one tool of the clinical armamentarium above any other. It is not our intent to attribute greater merit to laboratory service than that which it has earned. The laboratory is not a perfect tool! It's ability is far below the demands placed upon it by some of the clinical problems referred to it. But it does offer certain standards of measurement or of comparison which are of value! Human beings used to measure by the "hand" and weigh by the "stone". We now measure by the micron and weigh by the thousandth of a milligram. By so doing we have come near to understanding the structure of the physical universe and of that part of it which concerns us as clinicians, namely, the structures and functions of the human body and those of the agents which act upon it. That is the service of the laboratory; to measure and to weigh more finely, to offer standards for comparison, ultimately so fine that we can recognize beginning disease before it has developed so far that any

layman can recognize it and possibly even identify it.

In this type of laboratory service to the subacute, the chronic or the apparently normal person who goes to his family physician for periodic examination at definite intervals, certain conceptions are fundamental.

The first of these is the conception of *stimulus* and *response*. In medical parlance we call these *etiology* and *symptom* or *physical sign*. It is absolutely essential, at every step in the analysis of a clinical problem, to keep this distinction between etiology and symptom (or sign) clearly in mind. The clinical tool for the discovery of etiology is the family and past history; for the discovery of symptoms, the personal history; for the uncovering of physical signs, the physical examination. The laboratory adds to the physical signs and to the etiology. Chemical studies of blood and urine, the routine tests of blood and urine, gastric analysis, spinal fluid studies are merely massing up or adding to the symptoms and physical signs already known to the clinician. They are of value in giving a more complete picture of the case and in guiding symptomatic treatment but they prove dangerous if they focus the attention of the clinician on symptoms to the exclusion of etiology. I believe that this point is worth mentioning because it is a really practical danger and not an imaginary one. The failure on the part of the clinician to make the distinction between etiology and physical sign, to the exclusion of etiology, is apparent every day that we practice medicine.

The laboratory is searching for etiology when it concerns itself with bacteria. How often that is we all know. As compared with the number of procedures done in clinical laboratories for the discovery of further physical signs, the number of procedures for the discovery of etiology is insignificant. I will not say that the attention of the laboratory should be focussed on etiology but my opinion is that the laboratory could make its greatest contribution to clinical medicine, if the clinician would demand more often that attention be paid to any bacteria found whether in the urine, the feces, the sputum or in any other of the excretions or exudates. Unfortunately the laboratory cannot follow its own tendency in this matter. The demand must come from the clinician, unless the clinician sees fit to take the laboratory physician into consultation, in which case the laboratory worker has an opportunity to make the desirable suggestion. Such investigations into etiology should include a study of the comparative virulence of the organisms found and should lead to suggestions as to therapy, whether treatment should aim to establish immunity by the use of sera (passive immunity) or by the use of vaccines (active immunity).

This leads us to consider another matter of vital importance from the laboratory standpoint, namely, the "portals of entry" of disease. This is a matter of fundamental importance in any clinical case, but our perspective is lost very often when looking at a case from the numerous angles which have to be considered by the clinician. The importance of the "portal of entry" stands out in its true perspective when the case is considered from the labor-

atory standpoint. From this standpoint we are not concerned so often with hereditary factors in etiology nor with trauma but we are concerned immediately with the mucous membranes, namely, with the respiratory tract, the gastro-intestinal tract and the genito-urinary tract. Excluding heredity and trauma, etiological agents affect the body through these three tracts. I am speaking of physical diseases. In the case of mental diseases, not due to physical disease, but due to environmental situations, of course the portal of enfry is the sense organs, but we are not concerned with mental disease in this paper, nor with behavior problems such as delinquency, criminality, et cetera.

The upshot of these remarks is that the study of every clinical problem in the subacute, the chronic and preventative groups should involve a thorough study of the portals of entry. This means that the air we breathe, the food we eat and the care or lack of it that we take in matters of personal hygiene of the main portals of entry, should come under consideration in any adequate study of these classes of patients. Such studies are profitable both for the institution concerned and for the patient under observation. I might add that, in my opinion, no period of observation in such cases is complete or fair to the patient or the institution which does not include such a study.

With such attention, as I have indicated, directed to the portals of entry and to etiology we might expect to see the disappearance of such symptom complexes as "diabetes" and "essential hypertension," for example. There are many others but let us consider only these two. Each consists of a set of symptoms, physical signs and laboratory findings none of which says a word about etiology or about the portal of entry. Hence each is shrouded in darkness. Though far from knowing how to cure, we are much nearer an understanding or comprehension of such diseases as syphilis and tuberculosis for in each of these diseases we have the etiological agent; we know how to look for and often how to find the portal of entry; we can determine with some assurance the organs involved and we can ascertain to an extent their functional pathology.

This leads to some remarks on the subject of *disease* in general. All disease involves structure or form and description is couched in words which have to do with structure, whether gross or microscopic. I am omitting for the moment abnormal chemical reactions demonstrated by stains, though these have to do ultimately with abnormal physical or chemical structure or form.

All disease involves function or activity. A tissue becomes overactive or underactive or at times one and at other times the other. We say that such a structure is hyperfunctional or hypofuntional or dysfunctional (hyperkinetic, hypokinetic or dyskinetic). Such a structure is over-sensitive, under-sensitive or of alternating sensitivity; it is over-responsive, under-responsive or of alternating responsivity.

The structural, the functional and the etiological are fundamental in any description of disease. If we would keep this in mind we would soon have a classification of all diseases which

would be simple, definite and unequivocal. Every disease would have an anatomical "surname", a functional "middle name" and an etiological "family name".

The last few paragraphs may seem to have little relation to my topic. The connection is this. In most of our acute cases we see, at first, hyperfunctional symptoms. The laboratory should be asked to look for irritants whether they are bacterial or otherwise. Later, we see dysfunctional symptoms as the patient's reserves begin to fail and, finally, we see hypofunctional symptoms where the body is failing to respond. What the laboratory can do and what it should be requested to do should be regulated largely by these considerations whether the case be acute or whether it be chronic.

Prognosis and treatment, I believe, can be based upon the same considerations. I hope to see the time when drug action will be taught under the fundamental captions mentioned: first, the organ affected; second, the sort of effect produced, proceeding from irritation or stimulation to paralysis or inhibition of function. But more important than this, I hope to see the bacterial poisons isolated and studied in the same way and finally, in treatment, we ought to study the reverse action of curative sera, conferring passive immunity, and of vaccines, conferring active immunity.

The following is an illustrative case: *P. M.*, female, white, 54, single housekeeper, was presented for study. She has a long history of gastro-intestonal trouble dating back for 25 years. She has made the rounds of the clinics in several cities without relief. She complains of weakness, palpitation, feels as though she is going to die at times; a typical neurasthenic syndrome with certain psychasthenic features. She has distinct "air hunger". Her *basal metabolism* varies as follows: plus 872, plus 438, plus 272, plus 6, plus 68. Her *blood pressure* varies as follows: 170/100, 160/96, 174/90, 180/95, 146/88. Her weight is 110 pounds, which is 23% below normal for her age and height. *Urinalysis* showed 4 plus acid, one plus blood, 2 plus pus, 1 plus hyaline casts; later, three plus acid, rare pus cell, no indican; there was no fixation of specific gravity or of quantity (*Mosenthal*); *functional test* showed 60% in 2 hours, which is the lower limit of normality. In other words we were not dealing with a kidney lesion with resulting retention of metabolic poisons to account for the clinical symptoms.

We tried to multiply our symptoms on the side of a neurosis but without much result, as follows; the adrenalin test showed some evidence of unstable sympathetic nervous system with adrenal minus; the pituitrin test pointed to the thyroid plus with pituitary and sympathetic minus; the atropin test pointed to vagus minus; the pilocarpine test showed normal or diminished vagus irritability; thyroxin had no effect; sugar tolerance test showed overactive utilization of sugar (high tolerance) which points to overactivity in one or more of several locations. The ensemble shows a marked dysfunctional (dyskinetic) splanchnic nervous system. So far we have merely multiplied physical signs.

Our next attack was on the liver.

This was found to be underactive, 20% of the dye ("tetrachlor") remaining at the end of 15 minutes, 17% in one hour and 15 minutes, and 3% in two hours and fifteen minutes. This finding checked with the hemoclastic crisis test of Widal and Abrami (W. B. C. 8200, 8200, 8000). Here then we have an adequate source for the clinical picture. We appear to be dealing with a complicated intoxication due to failure of the de-toxicating power of the liver. But, having found the cause of our symptoms, we cannot pause because we know that the liver is never a *portal of entry* except by direct injury and by heredity. Neither exists in this case. The genito-urinary tract was ruled out. The respiratory tract was ruled out. The hemo-lymph system was ruled out except for a pair of old tonsils which the patient refuses to have removed. We are left, then, with our history of gastro-intestinal disorder of many years duration.

The examination of the stool reveals a foul, semi-solid specimen containing undigested fat and starch with 40% Gram positive bacilli and cocci. Here we seem to have our etiology in a pathogenic gastro-intestinal flora.

Treatment indicated is to change the flora in order to prevent further damage, but prognosis is poor as to repair of damage already done and is doubtful as to our ability to maintain a normal flora, though some progress has been made in this direction with good clinical results, so far.

Conclusion

I do not wish to extend this paper beyond reasonable length but I want to emphasize once more the importance of considering disease from the tripartite standpoint of the pathological structure, pathological function and etiology. Secondly, I want to emphasize the fundamental nature of the distinction between symptom and cause. Thirdly, I want to recall to your minds that the laboratory as now organized performs its chief service by multiplying physical signs for you. Fourthly, I want to bring a realization that the greatest future service of the laboratory will be in the field of etiology and of treatment.

Editorial

THE COMING MEETING IN NEW ORLEANS

At this time there is being shown an unusual degree of interest in the coming Clinical Meeting of the College in the city of New Orleans, during the week of March fifth; and the prospects of an unusually large gathering of Fellows and Associates seem certain. One hears from all sides anticipations or promises of attendance. No other meeting of the College has called forth so many expressions of eagerness and desire to attend as has this one; and for very good reasons. New Orleans has so much to offer of interest along so many diverse lines. The climatic change—the prospect of meeting an early spring on the shores of the Gulf, in the first week of March, is in itself a great inducement to the Northerner; and this alone will be sufficient to persuade some practitioners to drop their work for a week and seek a pleasant recreation in the real old South, where traces of southern history and manners still linger. And racial mystery and romance as well! New Orleans has a very individual atmosphere and flavor—almost that of a foreign city. A visit to it gives the same thrill of discovery and surprise as going abroad. It has not yet been fully Americanized. The city has been described as "a Parisian who came two centuries ago to the banks of the Mississippi, and has never cared to return to her mother country." Perhaps no other characterization of the Crescent City couid be so apt as this one—the city of the French adventurers—of the Creole—of the Mardi Gras—the Old Ursuline Convent—memories of the old French Opera—the Creole balls—and the old restaurants—the old cemeteries—these reminders of its two centuries of history betray its Gallic origin and spirit. All of this story of the city's past has been most charmingly told by Grace King in her book "New Orleans, The Place and the People," of which the Macmillan Company put out a new edition in 1926. A native, herself, she tells the fascinating tale of New Orleans with love and sympathetic understanding of the city and its people, throughout the whole period of its history, from the early discoveries and exploration of the Mississippi river, through the colonization of Louisiana and the founding of New Orleans, the French immigration, the Spanish domination, the American purchase and control, the episodes of Lafitte and Jackson's victory, antebellum days, the Civil War, down to the modern period of development. The interesting story is told in a charming personal manner as of a personal recollection, projected against a background of historical development, with here and there lurid gleams of early slave days, the buccaneers, old Creole times, the social

menace of the quadroon, duels under the oaks, and the savage superstitions of voodism still persistent. Not omitted are the great epidemics of cholera and yellow fever when year after year the specter of death lurked in the city. In 1853, out of a sixty thousand population, forty thousand were attacked and eleven thousand died of yellow fever. In 1854 and 1855 the fever returned with cholera with a death rate of seventy two and seventy three per thousand. Look up in your library the contemporary accounts of these epidemics in the medical journals of those years. Within our generation medicine has seen the conquest of these great plagues, and New Orleans happily will never again know the constant menace of death as experienced by its inhabitants during the first three quarters of last century. We strongly advise the reading of Grace King's book to any one planning to visit New Orleans. From no other single volume can so much of the soul of New Orleans be obtained. Its charming little illustrations will also indicate the architectural and historical bits one will wish to search out. With this book in hand delightful sallies of exploration into the *vieux carré* may be made from the headquarters hotel. And there are other attractions in these explorations of street and alley, old furniture, old ironwork, and other relics of Creole days may still be picked up, even an occasional book or two of interest. There are also the restaurants where characteristic Southern and Creole food is still served offering fine opportunities for gastronomic adventures. Advice from a native citizen is to this effect—"Take your breakfasts in the hotel, but go to various of these characteristic restaurants for other meals." A complete exploration of city, the river front, the residential portions and the old cemeteries will occupy a large part of the time not taken up by the meetings, or all of it, according to how thoroughly one studies the city. Several days should, however, be added to the five days of the meeting, in order to do it well; and any one who can accomplish this will surely be well repaid for the extra time spent. In addition to Grace King's book, there has recently been published by Doran an "Impressions of Old New Orleans in Pictures" by Arnold Genthe, conveying artistically the charm and beauty of the remaining bits of the old city, and this we advise you to study before you go to New Orleans, and then, when you are there, to search out similar bits of architectural beauty in the old courts and alleys, in the lights and shadows of arch and balcony, stairway and ancient walls. If photography is one of your hobbies here is a rare opportunity to collect visual impressions of real pictorial value. Perhaps you have been told that New Orleans has been ruined artistically by its rapid modernization—that the old things are gone, the old buildings destroyed, the old French Opera House burned and other like discouraging things. Some of this unfortunately is true, but the work of destruction of the old and beautiful has been halted in time to save much that still makes New Orleans unique among our cities. In the *vieux carré* the spirit of the old Creole life may still be found if one looks for it. And

then if you do recapture it you will understand the soul of New Orleans in its significance to the rest of American cities—it was France transplanted to the wilderness of swamp, bayou and mighty river—France it remained through the Spanish domination—purchased by the United States, over a century of American ownership and transforming influence has not yet effaced its hereditary characters. New Orleans offers us still the charm of ancestral foreign manners and customs to a greater degree than any other city within the bounds of the United States. The great and menacing river upon, or perhaps we should say beneath, whose shores the city is built will be of especial interest to every visitor to the city. The second greatest port in the country, its docks constitute a wonderful water front of over twenty miles. There are said to be many interesting river excursions available. The shore of the Gulf, with its summer houses, bathing beaches and pine forests also offers other opportunities for pleasant recreation. We are saying so much about the attractions of New Orleans as a fascinating city that we are neglecting perhaps the medical side of the meeting. A glance at the program will convince the Fellows of the College that there has been prepared for them a notable set of lectures and addresses by well-known internists, and that these presentations will offer new aspects and phases of the problems connected with cancer, the anemias, tuberculosis, cardiac disease, epilepsy, abnormal metabolism, diabetes and the infectious diseases. These contributions have been logically arranged in groups in the program and it is certain from the character of the men presenting these that all of the papers will be up-to-date vital presentations of the subjects chosen for these symposia. A definite effort has been made to make of the morning and evening sessions post-graduate courses in the best meaning of that somewhat overworked phrase. Instead of a confusing mixture of subjects each session will have a well-defined entity of subject and treatment, and in this respect it is hoped that the listeners will be able to carry away with them more clear concepts of the subject matter than is usually possible under the confused and hurried manner in which most so-called post graduate courses are conducted. Two especially notable features stand out on this program. Dr. Julius Bauer of Vienna will present the opening address of this meeting. He holds now the recognized position of being one of the foremost thinkers in internal medicine, and his views on constitutional pathology have made him perhaps the chief European proponent of the modern philosophy of medicine. His address and clinics will in themselves secure for this Clinical Week a degree of prestige not equalled in any of the previous meetings. We must again call attention to the clinics offered by the local profession. In them there will be presented an abundance of clinical material peculiar to the Gulf Region, and the visitors will have a wonderful opportunity of becoming acquainted with a variety of subtropical diseases at first hand. The opportunity to visit the Leper Colony is another medical opportunity not to be overlooked.

Abstracts

Antirachitic Effect of Skyshine. By FREDERICK F. TISDALL and ALAN BROWN (American Journal of Diseases of Children, November, 1927, Volume 34, pp. 737-741).

The term skyshine is used to designate the sun's rays that are reflected from the sky and clouds in contradistinction to the rays received directly from the sun itself. An object placed on the sunny side of a street receives rays not only from the sun but also reflected rays from the sky. On the shady side of the street only the rays reflected from the sky (skyshine) are received. If the object is again placed on the sunny side of the street and if a long cylinder pointed directly at the sun is placed over the object, the rays from the sky are cut off by the walls of the cylinder, and only the rays directly from the sun pass along the inside of the cylinder to the object at the bottom. No previous studies of the antirachitic effect of skyshine have been recorded. In 1920, Dorno reported that when the sun is at its height in the sky, the reflected ultraviolet rays from the sky (skyshine) are 15 per cent greater in amount than the ultraviolet rays received from the sun directly. According to Dorno, then, if an object is placed on the shady side of the street with the sun at its height, the object will receive 15 per cent more ultraviolet radiation than if it is placed at the bottom of a cylinder which cuts off the skyshine and allows only the direct rays of the sun to fall on it. The authors carried out a series of experiments on rats to determine the antirachitic effect of skyshine. As a result of their investigation they conclude that the antirachitic effect of sunshine (reflected rays from sky and clouds) is approximately from one-half to two-thirds as great as that produced by what is ordinarily termed sunshine (rays from the sun plus the reflected rays from the sky). Reddening of the skin by ultraviolet rays is not a suitable unit for the measurement of ultraviolet therapy. It should be regarded simply as an accompanying phenomenon which may or may not be a measurement of ultraviolet rays received.

The Effects of Measured Amounts of Ultraviolet Radiation on the Blood Count of Normal Rabbits. By MARY HARDY (American Journal of Hygiene, November, 1927, Volume VII, pp. 811-837).

The conclusions of this investigation are summarized as follows: Single radiations from a quart mercury arc, in doses from 12 to 48 lithopone units of ultraviolet energy, produce no change in the erythrocyte count in normal rabbits. Successive daily doses of 12 L. U. for eight days had no effect on the red count during the radiation period. After radiation was discontinued there was a slight rise which lasted for about a fortnight. The platelet count was increased by single doses of radiation, the rise varying directly with the amount of ultraviolet energy given. Successive daily doses increased the amount progressively, so that the extent and duration of the rise was greater than that following any single dose. The immediate effect, both with single and successive doses, was a short drop which was followed by the marked rise above normal. Successive small doses, of 12 L. U. for eight days, did not bring about any change in the white count. There was an initial drop in the lymphocytes, and, therefore, in the total count, within an hour after radiation, but the count was normal the next day. An initial drop in the lymphocytes is a constant reaction to all ultraviolet radiations given in single and in successive daily doses. Variation in the amount of radiation has little effect on the

extent of the drop, but the duration is directly proportional to the dose. After a massive single dose of 96 L. U., the lymphocytes remain below normal for several days. Ultraviolet rays, shorter than 300 mμ, produce an increase in lymphocytes, following an initial drop, provided the dose is not too great. The rise reaches a maximum two or three days after radiation. The maximum increase is probably caused by a specific amount of ultraviolet energy. Under the conditions of this experiment the optimum dose was about 24 lithopone units. Heavy radiations of the region of wave lengths shorter than 275 have no effect on the polymorphomuclears, but rays between 275 and 320mμ produce a sharp rise in these cells which reaches a maximum in about five hours. The increase above normal lasts for several days, and is proportional to the energy of ultraviolet radiation in the region between 320 and 275 mμ. The changes in the blood cells observed in this investigation were in no case phenomenal. It must be pointed out, however, that the animals were all normal and living under ordinary conditions of food and environment. Animals kept in the dark, or having a low blood count to begin with, would probably respond more readily to radiation than would a normal rabbit. Since ultraviolet radiation has been used so extensively in the treatment of rickets, investigations have shown that irradiation of normal animals does not bring about an increase above normal in the blood calcium or phosphorus. It is interesting, therefore, to have found consistent changes in the blood count subsequent to radiation of normal individuals. Radiation of individuals with low counts might be expected to produce more striking effects. The fact that only a narrow range of ultraviolet intensity is capable of producing a lymphocytosis corresponds to observations on other biological phenomena where short exposures are found to be stimulating and larger ones depressing. It has already been noted (Pena and Clark, 1924) that the growth of fungi is stimulated by short exposures and depressed by large ones. Unpublished work by O'Donnell has shown increased irritability of melanophores after a short exposure, with a maximum irritability for a certain definite dose. Stronger doses resulted in a decrease in irritability and eventually death. In the same way a definite amount of ultraviolet energy produces a lymphocytosis, but for larger exposures, the initial drop lasts for a number of days, giving a lymphopenia. This suggests that in the therapeutic use of ultraviolet radiation there may be an optimum dose and that greater doses may be useless or even harmful.

Analysis of Morphological Blood Changes in Pernicious Anemia Following Administration of Liver. By CHARLES H. WATKINS and HILDING BERGLUND (Proc. Soc. for Exper. Biology and Medicine, December, 1927, XXV, p. 206).

The introduction by Minot and Murphy of liver diet in the treatment of pernicious anemia has supplied experimental medicine with a hitherto unequalled method of studying blood formation. Three general types of anemia have been produced experimentally, secondary anemia due to hemorrhage, the aplastic anemia due to the destruction of the blood forming elements in the bone marrow and the hyperchromatic anemia produced by certain poisons. The fact which differentiates the condition in pernicious anemia from the types of anemia that have been experimentally produced, is that in pernicious anemia a blood is available which shows a low spontaneous regenerative activity and yet the bone marrow is not aplastic. Minot and his co-workers have shown that after about two months of the liver treatment, the morphological picture of pernicious anemia has returned to practically normal. Watkins and Berglund have made a detailed study of the morphological blood features in the case of a woman 52 years of age presenting the classical features of the disease. Before the liver diet (all liver given raw) the morphological picture was studied for 5 days. At the time the liver diet was started the total number of normoblasts per

cu. mm. of blood was 78. Immediately after the liver was started they increased rapidly so that by the 8th day the total number was 870 per cu. mm., after which there was a gradual decline until by the 16th day they had disappeared. The highest percentage for the normoblasts was 1015 on the 8th day. The reticulocyte curve began to rise 4 days after treatment was begun and reached its peak on the 15th day at which time the normoblasts had practically disappeared. The increase was 9,900 per cent on the 15th day. This represents the highest percentage increase of any of the formed elements. There was a slight secondary rise in the normoblast curve on the 13th day and a similar one occurred for the reticulocytes on the 23rd day. At first this was thought to be an individual variation, but it has since been seen in other cases. The total red count remained constant until the 6th day after the diet was started and then there was a marked increase up to the 18th day. From this time on the count rose more slowly up to normal. The increase in erythrocytes was about 410 per cent which was reached about 50 days after liver was started. Comparing these curves with the graphs of the reticulocytes, it will be found that at the time of the most rapid increase in the reticulocytes there is also the most rapid increase in total red cells. Although the reticulocytes offer a good means of estimating the regenerative activity of the bone marrow, they do not represent the only method of erythrocyte production. Thus the total reticulocytes increase to slightly over 600,000 per cu. mm., while at the same time the total red cells increase from below 1,000,000 up to more than 3,000,000 cells per cu. mm. Therefore, many mature red cells are being released from the bone marrow along with the less mature reticulocytes. During the liver treatment the eosinophiles increased from 2 per cent to 48 per cent of the total number of leucocytes; the eosinophilia begins after the peak of reticulocytosis has been reached, and at the time the rapid increase in the red cells has diminished. Although the morphological blood picture returned to normal following the liver treatment, the so-called "pernicious anemia neutrophiles" remained. This was observed in other cases also. Whether this deviation from the normal will ultimately disappear has not been established, but it is of aid in the diagnosis of pernicious anemia after the blood picture has become essentially normal. The authors conclude that megaloblasts are not essential in the diagnosis of pernicious anemia. Liver diet causes a response in the circulating blood in the form of an appearance of normoblasts, reticulocytes, mature erythrocytes and eosinophiles in the order given. The progressively increasing eosinophilia may be an expression of an overdosage with liver.

Reviews

Diseases of the Mouth. By STERLING V. MEAD, D.D.S., Professor of Oral Surgery and Diseases of the Mouth, Georgetown Dental School; Professor of Diseases of the Mouth, Georgetown Medical School; Oral Surgeon to Georgetown Hospital; Dental Surgeon to Providence Hospital; Consulting Oral Surgeon to Casualty Hospital; Consulting Dental and Oral Surgeon to Shady Rest Sanitarium; etc., Washington, D.C. 578 pages, 247 original illustrations in the text and 29 full page color plates. The C. V. Mosby Company, St. Louis, 1927. Price in cloth, $10.00.

The author states that the preparation of this work upon diseases of the mouth has been prompted by the conviction gained from the teaching of both dental and medical students and from a large consultant practice, of the constantly growing need for a more intimate co-operation between dentists and physicians in the effective handling of the intricate problems of oral sepsis and other affections of the mouth which, if not intelligently diagnosed and treated, may affect disastrously the general health of the patient seeking dental or medical relief. The volume has been written primarily as a textbook for dental and medcal students, but the author hopes that it will also supply both dentists and physicians in the practice of their professions with the fundamental principles and practical knowledge necessary for their routine work in making a correct diagnosis of abnormalities within the mouth, and thus to permit them to give a correct prognosis, so that proper treatment may be applied more promptly and efficiently than in the past. In order to accomplish this the author presents a definite routine plan of procedure for the making of oral examinations, for the recording of the data so obtained, and for the future care of the patient, whether he be referred from the physician to the dentist or from the dentist to the physician for subsequent treatment. For this purpose the author has aimed to give his own personal experiences and observations rather than to quote from the writings of others. The literature has also been carefully examined, and the important references upon the various subjects discussed are given at the end of each chapter. The book has been profusely illustrated with drawings, photographs and radiograms as the nearest approach to personal clinical observations and individual contact in the teaching clinic. There are 34 chapters, the first sixteen of which are concerned with dental material chiefly: oral examination, radiograms, diagnosis of pulp vitality, transillumination of teeth and gums, bacteriologic examination, disorders of enamel, dentin and cementum, dentition, abnormalities of the teeth, malocclusion, saliva, dental calculus and accretions upon the teeth, impacted and unerupted teeth, peridental diseases, diseases of dental pulp, periapical diseases and pulpless teeth. The remaining chapters treat of infections of mouth, floor of mouth and neck, diseases of the blood, blood vessels and nerves involving the mouth, diseases of the lip, tongue, throat, salivary glands and ducts, maxillary sinus, congenital clefts of lip and palate, stomatitis, diseases of the mandibular joint and muscles of mastication, maxillary bones, tumors, cysts and relationship of oral sepsis to systemic disturbances. Many of the subjects are very superficially treated and its chief value would seem to be that of a large manual listing the various abnormal conditions without an adequate treatment of any one. The book is of much greater value to the dentist than to the physician because of this rather handbook method of superficial treatment. Likewise,

the many illustrations are chiefly of dental interest.

Nasal Neurology, Headaches and Eye Disorders. By GREENFIELD SLUDER, M.D., F.A.C.S., Clinical Professor and Director of the Department of Oto-Laryngology, Washington University School of Medicine, St. Louis. 428 pages, 167 illustrations including 2 color plates. The C. V. Mosby Co., St. Louis, Missouri, 1927. Price in cloth, $11.50.

Since the appearance of his monograph, in 1918, dealing with headaches and eye disorders of nasal origin, the author has become constantly more impressed with the neurological side of rhinology. He has chosen the above title for the present volume with the special intention that it may attract the interest of neurologists, internists and ophthalmologists to a greater extent than the customary treatise on rhinology. Rhinology greatly needs this cooperation for two very definite reasons, namely, in order to secure clinical cooperation in obscure neurological cases and in order to obtain post-morten material in which the life history of the individual is definitely known. Material for the study of the pathology involving these tissues is the most difficult of any to obtain, in fact, hithertofore it has been impossible to obtain. In the chapter on Some Neurological Problems special emphasis has been laid upon the neurological side of rhinology and the special part played by the involuntary nervous system which is superficial in the nose and nowhere else in the body. Most of the recent clinical and experimental work on the involuntary system has been reviewed in this chapter with the hope of exciting ideas in the minds of others concerning the nose and the involuntary system. In the volume are also included material of a purely rhinological interest, an antrum technique heretofore not published, a chapter on orbital abscess and one on anterior ethmoidal neuralgia. There are ten chapters, distributed over the following divisions of the subject: the minute pathological anatomy by Jonathan Wright; the nose; vacuum frontal neuralgia; the syndrome of nasal ganglion neurosis; hyperplastic sphenoiditis and its clinical relations to the environing nerves; some neurological problems in rhinology; surgery of the maxillary antrum; orbital abscess and case histories. Eighty-three pages are given to this last chapter. The book is clearly and concisely written, the illustrations are largely from drawings showing anatomical relations or operative procedures, and are very satisfactory for the purposes for which they are designed. The lack of pathological material upon this subject is reflected in the lack of illustrations concerned with the pathological basis. For that reason the discussion of the various clinical conditions appears somewhat empirical. The author recognizes this in the closing paragraphs entitled Afterthoughts. While believing that many cases of headache are caused by hyperplastic lesions of the post-ethmoidal-sphenoidal area, he does not hold thatt his lesion is the explanation of all cases. The whole discussion is clouded by the question as to whether any adult in the temperate zone is free of this lesion.

International Clinics. A Quarterly of Illustrative Clinical Lectures and Especially Prepared Original Articles on Treatment, Medicine, Surgery, Neurology, Pediatrics, Obstetrics, Gynecology, Orthopedics, Pathology, Dermatology, Ophthalmology, Otology, Rhinology, Laryngology, and Hygiene. By Leading Members of the Medical Profession Throughout the World. Edited by HENRY W. CATTELL, A.M., M.D., Philadelphia. J. B. Lippincott Company, 1927. Vol IV, Thirty-seventh Series. Price in cloth, $3.75.

This volume contains thirty-five articles, twenty-five of these being "Travel Clinics" representing well-known clinicians of London, Edinburgh, Frankfort, Hamburg, Copenhagen, Stockholm and Oslo. There are three articles on Diagnosis and Treatment; two on Medicine; two on Surgery; one on Medical History and two on Post-graduate Study. There are 87 figures, two colored plates and numerous charts. The travel clinics consist of brief, interesting presentations of important subjects, and contain many valuable points and suggestions. Of

the American papers that by Hegner on the Clinical Diagnosis of Human Intestinal Protozoa is most timely in its scientific conservatism and should act as a control of the over-zealous and ignorant exploitation of human intestinal protozoan diseases that has been going on during the last several years. Harlow Brooks has also an exceedingly valuable practical article on The Treatment of the Patient with Pneumonia. Pugh's article on Stricture of the Urethra is also a valuable survey of the subject. Oliver's article on medical history, The Middle Ages, is interesting and entertaining.

Contributions to Medical Science; Dedicated to Aldred Scott Warthin. WILLARD J. STONE, B.S., M.D., F.A.C.P., Editor; and CARL V. WELLER, M.S., M.D., F.A.C.P., Professor of Pathology and Assistant Director of the Pathological Laboratories, University of Michigan, Chairman of the Editorial Committee. xxxii + 720 pages. Frontispiece and four special illustrations, 268 illustrations in text. Geo. Wahr, Ann Arbor, 1927. Price in fabricoid, carriage prepaid, $10.00.

The appearance of an American medical *Festschrift* must meet with the approval of all who believe that there is a soul in medical education; and that it is fitting for mature students of Medicine, many years removed from the day of their graduation, to honor one to whom they owe much of the shaping of their scientific destiny. Such tributes have become altogether too few in recent years so that the advent of the present volume assumes additional significance. A group of his earlier colleagues, and pupils of both earlier and later years have dedicated this collection of their original medical investigations to Aldred Scott Warthin, A.M., Ph.D., M.D., F.A.C.P., Professor of Pathology and Director of the Pathological Laboratories of the University of Michigan, and also the Editor of the *Annals*, in honor of his sixtieth birthday, October 21, 1926, and of the completion of his thirty-fifth successive year of teaching in the University. The editors have found it possible to have one or more representatives for each of the thirty-five classes which Dr. Warthin has taught. This unbroken sequence makes this volume almost unique among similar tributes. A Proem by Victor C. Vaughan and a Foreword by George Dock, both appreciative of Dr. Warthin's work in the University of Michigan, open the book. These are followed by fifty-four scientific contributions which are not arranged chronologically, as the purpose of the book might predicate, but are grouped according to their subject matter. Exception to this principal is found in the articles by G. Carl Huber, F. G. Novy and Peyton Rous, the first two early colleagues and the last at one time an instructor in Dr. Warthin's department. Huber describes a new method of fixing and staining central nervous system tissues for the purpose of studying cytoarchitecture. His paper emphasizes a method of approach which may be entirely new to many, the study of spinal cord tracts by means of microscopical sections in longitudinally oriented planes, running through several successive segments. Malcolm H. Soule collaborates with Novy in reporting some observations on the gas exchange of the bovine tubercle bacillus. The average respiratory quotient for this organism as grown on glycerol-agar was found to be 0.883; on glucose agar, 1.036; on serum agar, 0.852, and on plain agar, 0.888. Under the, to a pathologist, at least, intriguing caption of "Pathology and the Glare of the Future" to Peyton Rous includes both a plea and a prophecy—pathologists equipped with expert knowledge of fundamental science as well as first hand acquaintance with the processes of disease. A group of papers, dealing with Industrial Medicine follows. Alice Hamilton, in a most interesting survey, reviews the significant advances of the past fifteen years in the field of industrial toxicology. Carey P. McCord finds that the basophilic material in the red blood cells of laboratory animals to which benzol had been administered importantly exceeds the normal amount. Lyle B. Kingery describes the interesting occupational dermatomycosis, known among the packers of the Northwest as "fruit poisoning", as to etiology, symptomatology and pathology. Six articles on cardio-vascular physiology and pathology

provide a natural group. In the first of these Carl J. Wiggers reports a study of the genesis and mechanics of temporary ventricular alternation and in the second, pulsus alternans is considered from its clinical aspect by Roger S. Morris. A clinical study of 105 cases (from a total of 378) which showed upon electrocardiographic study a voltage not exceeding eight millimeters deflection in at least one of the leads I or II, is reported by C. T. Burnett with the collaboration of G. F. Pelz. The significance of such low voltages is discussed. George R. Herrmann demonstrates the electrocardiographic differentiation of primary from secondary dextrocardia, illustrating his thesis by three new cases of situs viscerum inversus totalis and contrasting the findings with those in three cases of the secondary type. Roentgenograms confirm the conclusions drawn from the electrocardiographic evidence. In view of Dr. Warthin's outstanding additions to our knowledge of cardiovascular syphilis it is not surprising to find that two contributors have chosen this subject. Interestingly enough, one of them, Harlow Brooks, presents the point of view of the internist in the treatment of this condition, while in the next essay an expert syphilographer, John H. Stokes, treats substantially the same subject matter, with additional observations on other forms of visceral syphilis. Cardiac pathology receives further consideration in the discussion of "Angina Pectoris and Coronary Occlusion" by Willard J. Stone. This article is based upon forty-six cases of coronary closure of which thirty-six came to autopsy. In a group of thirteen in which careful microscopical studies of the coronary vessels were made, syphilitic periarteritis was found in two instances. The histopathology of syphilis of the tonsil is described by Allen C. Starry. His photomicrographs are unusually good, especially those showing spirochetes. He finds that polymorphonuclear infiltration may characterize certain acute exacerbations of the syphilitic process. This brings tonsillar syphilis in accord, in this respect, with the similar infiltrations long known to exist in the syphilitic umbilical cord and with those which Dr. Warthin himself first described for syphilis of the myocardium. Thyroid disease is presented through a series of clinical observations by James Rae Arneill, and the management of patients with toxic goiter is described by Richard R. Smith. E. B. Potter emphasizes the importance of the "Graves' constitution (Warthin)" by an analysis of twenty-two cases of exophthalmic goiter in which necropsy examination of the thymus was made. Hyperplasia of the thymus as well as general lymphoid hyperplasia was found. Another generalized disease of the lymphoid tissue is considered by Carl H. Fortune who finds that gross visceral infiltrations in generalized lymphoblastoma occur most frequently in the kidney and liver. The clinical response, and calcium and phosphorus metabolism, of infants with idiopathic tetany and rickets, under the influence of parathyroid extract administration, is made the subject of report by Lynne A. Hoag and a group of associates. This group of articles is continued by D. Murray Cowie and John P. Parsons, who find that hay fever and pollen asthma can best be treated by combining administration of pollen extracts with such environmental changes as the nature of the sensitization may indicate. Ralph R. Mellon discusses the newer biology of the bacteria, the untenability of the old morphologic concepts and the growing importance attaching to "cyclostages" in bacterial growth. That it is the hemolytic streptococcus alone which determines mortality in small-pox is the belief of J. G. Cumming. As a corollary it follows that the practitioner, by resorting to laboratory procedures, can make an early and reasonably definite prognosis in all cases of this disease. C. W. Edmunds found physostigmine of practically no value in the treatment of botulism in laboratory animals. Results with Congo red were only slightly more encouraging, but he believes that such experiments point the way to ultimate success by direct chemotherapy, combined with antitoxin, morphine and artificial respiration. Four articles dealing with tuberculosis are grouped together. Lydia M. DeWitt summarizes the results of her experiments with complex gold salts in the

chemotherapy of tuberculosis in guinea pigs. Difficult points in the differential diagnosis of renal tuberculosis, with illustrative cases, are discussed by Carl W. Eberbach, and Francis E. Senear offers a very timely and helpful study of the general diagnostic importance of the tuberculides as frequently pointing to tuberculosis elsewhere in the body. From a consideration of the mechanism and physiology of artificial pneumothorax Warren C. Breidenbach concludes that this procedure should be applied to earlier cases than has been the custom in the past. Pneumothorax is recommended also by J. T. Watkins for certain suitable cases of lung abscesses, while for others bronchoscopy or pneumocautery drainage are the methods of choice. The value of Litten's phenomenon in determining the activity of the diaphragm and also that of the lung is the subject of Warren P. Elmer's contribution. Frank Smithies discusses parasitosis of the biliary tract and reports thirty-seven instances of protozoal infestation and one of *Necator americanus*. He believes that these conditions are of etiologic importance in a considerable variety of digestive disturbances. Variations in urobilogen output throughout the day and as affected by the taking of meals and by purgation are discussed by George B. Wallace and J. S. Diamond. These variations may affect the interpretation of this test as an index of liver function. H. S. McGee reports the results of an interesting study of bile secretion made upon a patient with biliary fistula. The ingestion of bile caused approximately a fifty per cent increase in the bile output. Three cases of oesophageal diverticulum form the basis of C. T. Sturgeon's paper. These were treated without a fatality by the two-stage operative procedure. Walter M. Simpson adds a new case and analyzes 150 human cases of aberrant pancreas found in the literature. Important clinical considerations are pointed out, such as the great frequency with which these aberrant glands are mistaken for neoplasms and their relationship to intestinal obstruction and intussusception. C. F. Tenney believes that gastric ulcers of types one, two and three of Cole's X-ray classification, properly belong to the internist rather than to the surgeon. He utilizes the Smithies regime in the treatment of such ulcers. Five cases of diabetes, studied by W. M. Brace for periods of from thirty-two to forty-five months, failed to show under insulin administration any gain in total glucose tolerance. Insulin was found to have no more ability to arrest the downward progress of the disease than the earlier treatment without the drug. Each patient lost tolerance during the period of treatment with insulin. F. C. Hyde emphasizes the uncertainty of gross pathological diagnosis in the differentiation of new growths. Methods for the production of experimental oedema are described by Samuel R. Haythorn and the importance of such oedemas in studies on anthracosis, pigment phagocytes, the histogenesis of the tubercle and on the origin of the Langhans' giant cell is discussed. Warren to Vaughan describes the behavior of the omentum in the presence of particulate foreign matter, including dead germ substance, in experimental animals killed at intervals up to thirty-six days. A 1 to 800 aqueous solution of Janus green is recommended by Stuart Wilson as a selective stain for renal vessels and glomeruli. Air dried frozen sections are used following arterial injection. The lobular architecture of the spleen is described and figured by Ward J. MacNeal and by serial sections he demonstrates the existence of multiple or compound lobules. Splenic pathology is represented by Luther F. Warren's contribution describing a new case of Gaucher's disease. He also adds five new cases from the literature to the forty-nine tabulated by Cushing and Stout. Carl V. Weller discusses the phagocytosis of melanin in a case of generalized melanoblastoma. The reticulo-endothelial apparatus appears to exercise a selective phagocytosis for the precursors of melanin. The chemical composition of normal sweat and that from patients with senile eczema and with psoriasis has been studied by R. E. Barney. Differences in the amounts of nitrogenous substances and chlorides seem significant. No uric acid was found in twenty-nine specimens. A group of papers of surgical interest follows.

Carl E. Badgley describes, with X-rays of illustrative cases, the two-stage transplantation of fibula for tibia. Harold K. Faber writes most interestingly of craniosynostosis (oxycephaly and allied conditions) and recommends before the third year of life the excision of the synostosed sutures as the only means practicable for the conservation of vision. The history of total rhinoplasty is well told by Ferris N. Smith who also gives his own method for this procedure. Blood culture is considered by Harold T. Lillie to be the most important laboratory aid in the recognition of involvement of vessel walls and the blood stream in otitis media. Methods of handling such cases are discussed. R. B. Canfield and A. C. Furstenberg discuss the diagnosis of laryngeal carcinoma and give their method for laryngectomy under local anesthesia. That massive leakage of cerebro-spinal fluid may follow lumbar puncture is shown by a case detailed by Lester M. Wieder, in which there was good reason for believing that this was the deciding factor in the fatal outcome. The patient, however, had lues of the central nervous system, including the pituitary body. Theophile Raphael and Robert R. Dieterle describe a case showing the Korsakow syndrome, apparently in association with epidemic encephalitis, and John L. Garvey gives the history with autopsy findings of a patient with adeno-carcinoma mucosum of the parotid gland in whom generalized metastases caused the clinical picture to be dominated by an extradural spinal cord tumor syndrome. The two cases of adamantinoma of the pituitary region forming the basis of the paper by Max Peet offer an interesting study in contrasts, one being typical of the Fröhlich type while the other was of the Lorain group. Hugo A. Freund gives a clinical case in which high values for blood urea, non-protein nitrogen, creatinine and uric acid seemed to indicate a serious nephropathy. Only late in the disease was a brain tumor recognized and autopsy showed this to be the only significant pathological process present. An appendix to the volume gives a complete Aldred Scott Warthin bibliography up to October, 1926. While there can be no unity in a book of the nature of the one under review, beyond that of the purpose in the minds and hearts of its contributors, it is evident that each one has written in an untrammeled manner of the subject in which he was most interested. The average of the resulting contributions is distinctly higher than that found in current medical periodicals.

C.V.W.

College News Notes

DR. A. S. WARTHIN HONORED

By Publication of Volume of Contributions by Colleagues and Former Students

In recognition of his thirty-five years as an outstanding teacher in the Medical School, and his international reputation as a pathologist, Dr. Aldred S. Warthin has been the recipient of an unique honor from his colleagues and former students, in the form of a volume entitled "Contributions to Medical Science." This book of 715 pages includes contributions from sixty-four authors, representing not only five of his early colleagues, Vaughan, Dock, Novy, Huber, and Rous, but also from one or more representatives from each of the thirty-five successive classes, who in the words of the editors, "has been proud to acknowledge Dr. Warthin as the greatest living teacher of pathology."

It was about eighteen months ago that a group of the medical alumni of the University got together and planned this volume in honor of Dr. Warthin's sixtieth birthday, October 21, 1927, and of the completion of his thirty-fifth year of teaching. The volume just published marks the completion of their labors. In one respect it is unique in *Festschriften* of this character because of unbroken sequence of papers coming from members from each of the thirty-five classes that have sat under Dr. Warthin.

On Tuesday afternoon, December 13, the formal presentation of the volume was made to the recipient. The opening address by Dean Hugh Cabot of the Medical School was as follows:

"It is characteristic of the Anglo-Saxon that he is generous in his commendations and appreciations of scientific men in other lands. He is likely to be very liberal in praise of his scientific brethren in his own country particularly if they live at a distance and he rarely sees them, but he is emphatically not liberal in voicing his appreciation of his immediate colleagues and he rarely ventures to praise them if there is any danger that they may hear it. This perhaps springs from a fear of embarrassing them, from a fear of awakening in them emotions which they habitually suppress or from other laudable but mistaken motives.

"Be that as it may, the fact remains that we do rarely indulge ourselves in the luxury of telling our colleagues what we really think of the greatness of their work and the great effect they have produced in their field, both through their contributions and their teachings.

"It is, therefore, somewhat notable that we have come here this afternoon to behave in a most un-Anglo-Saxon fashion. We are about to give ourselves the pleasure of telling our colleague, Professor Warthin, how much we appreciate the amount, variety, and importance of his contributions to science and how well we recognize his skill as a teacher and the widespread and permanent effects which he has produced in advancing sound medical education. There is no one of his colleagues who can more skillfully throw off the cloak of our reticence and state more knowingly and appreciatively our true estimate of his value than his old friend and colleague, Professor Novy, and he will, therefore, make the presentation."

The formal presentation was then made by Dr. Frederick Novy, '87, a colleague of Dr. Warthin from the first.

"The Committee in charge has delegated to me the privilege and honor of acting in their behalf on this rare occasion. I appreciate this privilege the more so since it has been my good fortune to have known Dr. Warthin from the time he was a freshman on this campus.

"Dr. Warthin came to Michigan from Indiana University where he had been under the inspiring influence of two enthusiastic and great scientists, Dr. David Starr Jordan, who later became president of Leland Stanford University, and the late Professor Eigenman. It was at Michigan that he obtained an A.M. in 1890, and his Ph.D. in 1893. It was here likewise that he obtained his medical degree in 1891.

"His service in the University began in 1891 when the Chair in medicine had been newly filled by the appointment of Dr. George Dock, who with his unusual training in Internal Medicine and Pathology and because of his rare diagnostic ability was destined to become one of the great teachers of Medicine. Under him, Dr. Warthin served first as Assistant, then as Demonstrator of Internal Medicine. The stimulus that he then received is seen in the fact that while with him he spent three consecutive summers, 1893-1895, abroad in the study of medicine and pathology.

"In 1895 when the chair of pathology was vacated, Dr. Warthin was appointed Instructor in Pathology and served as such until 1899, when he became Assistant Professor. He was made Junior Professor in 1902 and finally, in 1903, Professor and Director of the Pathological Laboratory, which position he has held ever since.

"During all these years, nothwithstanding the strain of teaching and of routine, Dr. Warthin followed his natural bent as an investigator and observer. It is impossible to mention here all of his publications. Suffice it to say that his studies on Hemolymph Glands, Blood-forming Organs, Anemias, Tuberculosis, Syphilis, Neoplasms, not overlooking his contributions to medical history, have won him his place in the front rank of American pathologists.

"Last year (1926) saw the completion of thirty-five years of service in this University. During that period over 3,000 students received the impress of his earnestness, and thoroughness, and of his devotion to science.

"It is a custom somewhat rare in this country, but less so abroad, for former pupils and associates to honor a great teacher and investigator by dedicating to him a Festchrift or Jubilee volume. It has been deemed appropriate to commemorate the thirty-five years of service and the 60th Anniversary of Dr. Warthin by a like observance.

"Dr. Warthin, on behalf of the committee in charge, I take the very great pleasure of congratulating you and presenting you with this volume which is dedicated to you. It contains contributions from your associates and from one or more pupils from each of the thirty-five classes which sat under your instruction. Accept it as an outward expression of the deep appreciation and respect of your old students and friends together with the hope that for many years to come you may carry on in full strength and vigor."

Dr. Warthin, accepting the volume, said:

"It is difficult to control one's emotion at such a time. No greater honor can come to a teacher than such tangible evidences as contained in this volume that his life-work has met with a fair measure of success, and that his teaching ideals have, in part at least, been justified. That so large a group of my old students could thus come together in such a notable demonstration of their creative interest and ability and of the possession of higher ideals of their profession than that of mere success in practice, make me most happy and very proud of the thirty-five classes that have passed through my department. Still happier am I when I realize that this number is only a small proportion of my old students who are showing such ideals and ability for creative living, but out of necessity could not be added to the group represented in this volume. I can claim, however, only a small share in this result; it is collectively a product of the labors and ideals of my colleagues during these thirty-five years. The Medical School and the University as a whole may well be proud of its medical graduates. To my old students who planned and carried out this volume, to its editors, and to my old teachers and colleagues who have contributed to it, I give my most sincere thanks for this, the greatest honor of my life."

In addition to the fifty-seven articles included in this handsome volume an appendix, prepared by Dr. Carl V. Weller, presents a long list, filling some eighteen pages, of books and articles by Dr. Warthin, as well as his contributions to periodicals. Nothing could indicate so impressively the real accomplishment of Dr. Warthin in his chosen field. The volume itself is beautifully printed and profusely illustrated, with a portrait of Dr. Warthin as a frontispiece.

The list of medical alumni who contributed to the volume are by classes, as follows:

1892, Richard R. Smith; 1893, Alice Hamilton; 1894, James Rae Arneill; 1895, Harlow Brooks; 1896, David M. Cowie; 1897, George B. Wallace; 1898, Lydia M. DeWitt; 1899, R. Bishop Canfield; 1900, Fritz C. Hyde; 1901, Charles W. Edmunds and Willard J. Stone; 1902, Harry S. McGee and Roger S. Morris; 1903, James G. Cumming and Warren P. Elmer; 1904, Samuel R. Haythorn, Frank Smithies, Charles T. Sturgeon, and Charles F. Tenney; 1905, Hugo A. Freund and Ward J. MacNeal; 1906, John T. Watkins and Carl J. Wiggers; 1907, Charles Stuart Wilson; 1908, Clough T. Burnett; 1909, Ralph R. Mellon and Luther Warren; 1910, Max M. Peet and Ferris N. Smith; 1911, Harold K. Faber; 1912, Harold I. Lillie, Carey P. McCord, and John H. Stokes; 1913, Carl V. Weller; 1914, Francis E. Senear; 1915, Albert C. Furstenberg; 1916, Carl W. Eberbach, Lyle B. Kingery, and Warren T. Vaughan; 1917, Warren C. Breidenbach; 1918, George R. Herrman and Lynne A. Hoag; 1919, Carl E. Badgley, Theophile Raphael, and John Purl Parsons; 1920, John L. Garvey; 1921, Robert E. Barney and Allen C. Starry; 1922, Lester M. Wieder; 1923, William M. Brace and Robert R. Dieterle; 1924, Walter M. Simpson; 1925, Eugene B. Potter; 1926, Carl H. Fortune.

The selection of the articles and the task of publication of the book was under the direct editorial supervision of Willard J. Stone, '01*m*, Pasadena, Calif., and Carl V. Weller, '13*m*, Professor of Pathology in the Medical School. The book was published by George Wahr, Ann Arbor.

A Tribute After Thirty-five Years' Service

Few American teachers have been so honored by their colleagues and former students as has Dr. Aldred S. Warthin in the recently published "Contributions to Medical Science" issued as a tribute to his thirty-five years of service as a pathologist and teacher. Such volumes have been rare in America, though in the past they have not been uncommon in Germany, where it has been customary to honor outstanding teachers by the publication of *Festschriften* such as this. A similar volume was issued by the Medical School some years ago in honor of Victor C. Vaughan's long service to the University, and to medicine, while at Johns Hopkins, Dr. J. H. Welch and the late Sir William Osler were similarly honored.

It is safe to say, however, that very few *Festschriften* either in Europe or America have been so beautifully and elaborately produced, or so completely representative of the recipient's career as this one, containing as it does contributions from every class that has filled in their autopsy protocols under his watchful eye. Similarly it is significant that many of these contributors are among the most outstanding medical teachers in America.

The above report and editorial comment were taken from the Michigan Alumnus of January 7, 1928. The volume is reviewed from a scientific standpoint in this number. Both notices and review have been made at the request of a number of members of the College. Of the contributors to the volume the following are Fellows of the College:—Hugo Freund, Detroit; John T. Watkins, Detroit; C. S. Wilson, Detroit; Harlow Brooks, New York; Ward J. MacNeal, New York; C. F. Tenney, Jr., New York; Luther F. Warren, New York; Willard J. Stone, Pasadena; George Dock, Pasadena; S. R. Haythorn, Pittsburg. Frank Smithies, Chicago; Carl J. Wiggers, Cleveland; C. V. Weller, Ann Arbor; James R. Arneill, Denver; C. T. Burnett, Denver; F. E. Senear, Chicago; W. C. Breidenbach, Dayton, Ohio; W. M. Simpson, Dayton, Ohio; and George R. Herrmann, New Orleans.

Dr. Oscar B. Hunter (Fellow, February 24, 1926), Washington, D. C., Professor of Bacteriology and Pathology and Assistant Dean of the George Washington University Medical School, was recently elected the new head of the District Medical Society. Dr. Hunter is also the Pathologist to the George Washington University Hospital and Dispensary, consulting Pathologist to the Casualty, Montgomery County and Sibley Memorial Hospitals, as well as Professor of Bacteriology and Pathology at the Central training School for Nurses.

OBITUARY

Dr. Albert Robin, Wilmington, Delaware (Fellow, March 10, 1923). Died December 23 of heart disease; aged 53.

Dr. Robin received his medical degree from the University of Pittsburgh School of Medicine in 1897 (then the University of Western Pennsylvania), and after pursuing postgraduate study at the Massachusetts General Hospital and at the Johns Hopkins University School of Medicine, moved to Wilmington and began his practice. He was known as the father of Wilmington's water filtration system and medical director of Hope Farm, the Delaware Anti-Tuberculosis Society's sanitarium. He was professor of pathology and bacteriology at Temple University School of Medicine from 1902 to 1907, director of pathology and bacteriology of the Delaware State Board of Health from 1899 to 1903, bacteriologist of the City Water Department in 1903, executive secretary of the Delaware State Tuberculosis Commission, and chairman of the medical board of the Physicians' and Surgeons' Hospital of Wilmington.

Dr. Robin was a member of the American Society of Bacteriologists, the American Public Health Association, the National Tuberculosis Association, the American Medical Association, the Delaware State Medical Association, the New Castle County Medical Association, assistant editor of the Atlantic Medical Journal and a member of the Board of Governors of The American College of Physicians.

BOARD OF REGENTS MET AT MEMPHIS

The Board of Regents of The College met at Memphis, Tenn., November 12th and 13th, just preceding the annual meeting of the Southern Medical Association at the same place. Members of the Board who were present include Drs. Smithies (presiding), Brown, Jennings, Clement R. Jones, Lucas, Martin, Morgan, Murray, Piersol, Roberts, White, Marriott, Warthin and Mr. Loveland (Executive Secretary).

Their deliberations extended over two days during which a host of business matters were transacted, College policies discussed and other important matters attended to.

Resignations Accepted

Resignations were accepted from the following, subject to the return of the membership certificate in the case of Fellows:

Fellows:

Thomas Alsop, Donald Frick, W. H. Lewis, George M. Niles.

Associates:

Arthur R. Gibson, Ben H. Huggins, Grant H. Laing, Alfred S. Maschke, V. A. Neel, Henry C. Sears, Frank E. Wiedeman.

Deaths Reported

Deaths of those whose obituaries appear elsewhere in this Bulletin were reported.

Fellowship Elections

The following applicants were elected to Fellowship:

Anderson, Wm. Willis.....Atlanta, Ga.
Baker, Gerdon E. .....Forty Fort, Pa.
Bass, Elizabeth .....New Orleans, La.
Bates, Lewis B. .....Ancon, Canal Zone
Bernhard, Robert .....New Orleans, La.
Bethea, Oscar W. .....New Orleans, La.
Blair, A. A. .....Fort Smith, Ark.
Boles, Russell S. .....Philadelphia, Pa.
Brosius, Otto T. .....Almirante, Panama
Campman, C. C. .....West Middlesex, Pa.
Castlen, Charles R. .....Seattle, Wash.
Clifford, Randall .....Boston, Mass.
Comstock, Carl R...Saratoga Springs, N.Y.
Crutchfield, E. D. .....Galveston, Texas
Cunningham, Robert L..Los Angeles, Calif.
Davison, Roland A...San Francisco, Calif.
DeSautelle, W. T. .....Knoxville, Tenn.

Duval, Charles Warren..New Orleans, La.
Elrod, J. O. .....Forsyth, Ga.
Eustis, Allan .....New Orleans, La.
Finigan, John J. .....Rochester, N. Y.
Fisher, Charles F. .....Brooklyn, N. Y.
Fleming, Wm. D. .....Washington, D. C.
Gregg, Harold W. .....Butte, Mont.
Hansen, Olga S. .....Minneapolis, Minn.
Hart, Wm. Lee .....Washington, D. C.
Heatley, John E. ....Oklahoma City, Okla.
Huber, Edward Godfrey.....Atlanta, Ga.
Hyman, Albert S. .....New York, N. Y.
Jacobs, Wm. F. .....Buffalo, N. Y.
Janjigian, Robert R. ....Wilkes-Barre, Pa.
Kahn, I. S. .....San Antonio, Texas
King, Hubert C. .....Lakewood, Ohio
Koch, Emil F. .....Brooklyn, N. Y.
Lamb, Ellis .....Clinton, Okla.
Lanford, John A. .....New Orleans, La.
Laubaugh, Ernest E. .....Boise, Idaho
Lepak, John A. .....St. Paul, Minn.
Levitt, Abel .....Buffalo, N. Y.
Lineback, Paul E....Emory University, Ga.
Loeber, Maud .....New Orleans, La.
McCall, Daniel Thompson ....Mobile, Ala.
McGovern, Louis .....Brooklyn, N. Y.
MacDonald, John A ....Indianapolis, Ind.
Matz, Philip B. .....Washington, D. C.
Mella, Hugo .....Washington, D. C.
Milliken, Herbert E. .....Portland, Maine
Morris, John M. .....Louisville, Ky.
Myers, J. Arthur .....Minneapolis, Minn.
Peters, LeRoy S....Albuquerque, N. Mex.
Podlasky, H. B. .....Milwaukee, Wis.
Pounders, Carroll M..Oklahoma City, Okla.
Retan, H. Walden .....Syracuse, N. Y.
Reynolds, Harold I. .....Athens, Ga.
Roberts, Edwin H. .....Fort Sill, Okla.
Rogers, Thomas E. .....Macon, Ga.
Roller, Robert Douglas.Charleston, W. Va.
Rucker, W. C. .....New Orleans, La.
Saxl, Newton Thomas....New York, N. Y.
Schaefer, Robert L. .....Detroit, Mich.
Shillington, M. A. .....St. Paul, Minn.
Silverman, Daniel N. ....New Orleans, La.
Snell, Albert Markley ....Rochester, Minn.
Steinwinder, C. D. ..San Antonio, Texas.
Stone, Charles T. .....Galveston, Texas
Tihen, Henry N. .....Wichita, Kan.
Welch, Stewart H. .....Birmingham, Ala.
Whitmore, Eugene R. ..Washington, D. C.
Wightman, Orrin Sage..New York, N. Y.
Wilson George H. .....Lexington, Ky.
Wyatt, Bernard L. .....Tucson, Ariz.
Wylder, Meldrum K..Albuquerque, N. Mex.

Resolutions Adopted

Among the more important resolutions adopted were the following:

Resolved, That the Chairman of the Board of Regents appoint a committeee of three to devise ways and means to further the endowment fund of The College as specified by the Constitution.

Resolved, That the four following recommendations of the Committee on Credentials shall be adopted in order to facilitate the work of that Committee:

1. Applicants who are not bona fide teachers or permanent laboratory workers shall be in the actual practice of medicine at a permanent location at least five years before being considered eligible for Fellowship.

2. The Committee on Credentials for Associateship of the Board of Governors shall hold conferences with the Committee on Credentials of the Board of Regents in order to correlate criteria and policies for admission to Associateship.

3. Applicants who fail to complete the requirements for admission to Fellowship within one year of date of filing applications shall be dropped, after suitable notification.

4. When an applicant has been in practice fifteen years or less without making any contribution to medical science, he should be requested to submit fifty histories and five autopsies, or a suitable thesis.

Resolved, That The American College of Physicians hereby endorses the project of the Gorgas Memorial Association.

ANNALS OF INTERNAL MEDICINE

In the report by the Editor, Dr. A. S. Warthin, to the Board of Regents at Memphis, announcement was made that the new journal of The College, Annals of Internal Medicine, is progressing satisfactorily and that although it is still late in appearance, several issues are almost ready for distribution. It is anticipated that the past numbers will all be distributed during December or the early part of January, and that thereafter all issues will appear regularly.

TWELFTH ANNUAL CLINICAL SESSION

NEW ORLEANS COMMITTEES

JOHN H. MUSSER, *General Chairman*

Committee on Arrangements

JOHN H. MUSSER — ALLAN EUSTIS
L. R. DEBUYS — ALDO CASTELLANI
J. M. BAMBER — GEO. R. HERRMANN
OSCAR DOWLING — HENRY DASPIT
C. C. BASS — I. I. LEMANN
RANDOLPH LYONS

Committee on Hall

GEORGE R. HERRMANN

Committee on Clinics

I. I. LEMANN, *Chairman*

C. C. BASS — L. R. DEBUYS
GEO. R. HERRMANN — RANDOLPH LYONS

Committee on Hotels and Transportation

J. M. BAMBER

Committee on Entertainment

HENRY DASPIT, *Chairman*

ALDO CASTELLANI — OSCAR DOWLING

Committee on Publicity

ALLAN EUSTIS, *Chairman*

C. C. BASS — OSCAR DOWLING

Exhibits

RANDOLPH LYONS

GENERAL INFORMATION

Headquarters: Roosevelt Hotel.

Registration headquarters, railroad office, information bureau, the commercial exhibit and the general assembly hall are all located here.

Inasmuch as the Clinical Session will be held only twelve days after the annual Carnival, Mardi Gras, and since this city is a most popular winter resort for vacationists, reservations should be made longer in advance than has been customary in other Convention Cities.

Who May Register—

(a) All members in good standing for 1928 of The American College of Physicians. (As usual, bills for membership dues will be distributed on January 1, for 1928.)

(b) All newly elected members.

(c) All applicants for membership in The College whose applications are still outstanding at the time of the Session.

(d) Members of the Orleans Parish Medical Society of New Orleans will be admitted to all general sessions as guests of The College and, in so far as space permits, will be assigned to special clinics, laboratory demonstrations, etc. (It is optional with them whether they secure Guest Cards at a fee of $5.)

(e) Qualified physicians who may wish to attend this Session as visitors and who pay the nominal registration fee of $5 and to whom "Guest Cards" are issued.

(f) Distinguished foreign visitors; physicians engaged in teaching or in scientific investigation; members of the Public Services of the United States, its possessions and Canada; retired practitioners of medicine and those who are pursuing studies in the various local colleges (in this group, all general meetings are open and, whenever possible, admission to special clinics and demonstrations will be arranged).

Blanks for all special clinics and demonstrations will be sent later with the program.

Reduced Railroad Fares:

Transportation to and from the New Orleans Clinical Session has been arranged on the Certificate Plan of fare and half fare. This applies to the railroads of the United States and the eastern part of Canada. Those who attend the Session will purchase going tickets at local railroad offices and at the same time request a "Certificate." This Certificate, when validated by the proper officer at the registration booth at New Orleans, will entitle members to purchase return tickets at half rate.

Reduced rates apply not only to members, but also to dependent members of their families.

Going tickets may be purchased from March 1st to 7th and the return tickets may be used up to March 13th. Those desiring to remain in New Orleans longer, in most instances, will be permitted to deposit their Certificates with the special railroad agent, Mr. W. H. Howard, located in the City Ticket Office of the Louisville and Nashville Railroad at New Orleans, upon

payment of fee of One Dollar ($1.00), and be able to use return tickets, with departure from New Orleans up to and including March 24th.

TENTATIVE PROGRAM

Monday, March 5th

Opening Session—2:00 o'Clock

1. Addresses of Welcome, Honorable Arthur J. O'Keefe, Mayor of New Orleans; Albert Bledsoe Dinwiddie, Ph.D., LL.D., President, Tulane University of Louisiana; C. C. Bass, Dean of the School of Medicine, Tulane University of Louisiana.

2. Reply to Addresses of Welcome, Frank Smithies, President of The American College of Physicians.

3. Julius Bauer, Vienna, Austria.

4. David P. Barr, St. Louis, "Multiple Myeloma."

5. L. G. Rowntree and George E. Brown, Rochester, Minn., "Studies in Blood Volume with the Dye Method."

6. Joseph Sailer, Philadelphia. Title not yet announced.

7. Frank R. Menne, Portland, Ore., "The Effect of Iodin on the Histopathology of the Thyroid Gland in the Instance of Hyperthyroidism."

Evening Session, Monday—7:45 o'Clock

1. Maud Slye, Chicago, "Cancer and Heredity."

2. J. L. Goforth, Dallas, "Natural and Acquired Body Resistance to Neoplasia."

Tuesday Morning, March 6—10 o'Clock

1. Dr. Charles T. Stone, "The Occurrence of Severe Anemia in Myxedema."

2. Dr. W. W. Duke, "Diagnosis and Treatment of the Anemias."

3. Dr. Hilding Berglund, "Liver Diet in Pernicious Anemia."

4. Dr. C. C. Sturgis, Dr. Raphael Isaacs and Dr. Millard Smith: "Treatment of Pernicious Anemia with Liver Fraction."

Symposium on Tuberculosis.

5. Dr. Charles L. Minor. Title to be announced.

6. Dr. F. M. Pottenger, "The Cause of the Varied Clinical Manifestations in Pulmonary Tuberculosis."

7. Dr. Gerald Webb. Title to be announced.

8. Dr. Robert S. Berghoff, "Intestinal Tuberculosis."

9. Dr. John W. Flinn, "A Study of the Differential Blood Count in One Thousand Cases of Active Pulmonary Tuberculosis."

Evening Session—7:45 o'Clock

1. Dr. James S. McLester. Title to be announced.

2. Dr. Allen K. Krause, "The Pathogenesis of Tuberculosis."

3. Dr. T. Z. Cason, "Some Unfinished Research Problems of the South."

Wednesday Morning, March 7—10 o'Clock

1. Dr. L. F. Bishop, "The Practice of Cardiology."

2. Dr. Morris H. Kahn, "Heart Strain and its Consequences."

3. Dr. J. P. Anderson, "Discussion of the Diagnosis of Coronary Occlusion with Special Reference to Its Simulation of Acute Abdominal or Other Surgical Conditions, with Illustrative Cases."

Symposium on Epilepsy

4. Dr. H. Rawle Geyelin, "The Relation of Chemical Influences, Including Diet and Endocrine Disturbances, to Epilepsy."

5. Dr. E. Bates Block, "The Relation of Organic Brain Disease to Epilepsy."

6. Dr. T. H. Weisenburg, "The Relation of Extra-cranial Disease to Epilepsy."

7. Dr. Tom Throckmorton. Title to be announced.

Evening Session—7:45 o'Clock

Symposium on Infectious Diseases.

1. Dr. C. E. Birkhaug, "Erysipelas."

2. Dr. A. R. Dochez, "Scarlet Fever."

3. Dr. Jean V. Cooke, Specific Prophylactic Measures in Varicella and Measles."

4. Dr. J. C. Small, "Rheumatic Fever."
6. Dr. W. M. Simpson, "Tularemia."

THURSDAY MORNING, MARCH 8—10 O'CLOCK

1. Dr. C. Saul Danzer, "The Pathogenesis and Treatment of Dyspnoea in the Light of Recent Experiments."

2. Dr. T. G. Schnabel, "A High Fat Diet in the Treatment of Migraine."

3. Dr. Henry Wald Bettmann, "Chronic Appendicitis from the View Point of an Internist."

Symposium on Diabetes.

4. Dr. Anthony Bassler, "Chronic Pancreatic Disorders, Diabetic and Non-diabetic."

5. Dr. Frederick M. Allen, "Present Results and Outlook of Jealetic Treatment."

6. Dr. A. A. Herold, "Diabetic Therapy, with Special Reference to the Newer Remedies."

7. Dr. W. H. Olmstead. "The Dietetic Management of the Diabetic in the Doctor's Office."

FRIDAY MORNING, MARCH 9—10 O'CLOCK

Symposium on Tropical Medicine.

1. Colonel Roger Brooke. Title to be announced.

2. Dr. Aldo Castellani. Title to be announced.

3. Dr. Wm. M. Jones, "The Early Lesions of Intestinal Amebiasis."

4. Dr. Bailey K. Ashford, San Juan, Porto Rico. Title to be announced.

5. Dr. Aristides Agramonte, Havana, Cuba. Title to be announced.

FRIDAY EVENING, MARCH 9—7:45 O'CLOCK

1. Dr. Julius Bauer, Vienna, Austria. Convocation Address.

The scientific program as given above will take about half of the time of the meeting. The remainder of the time will be occupied by clinics; In a general way these will be arranged as follows: In the afternoon from 1:45 to 4:30, clinics will be held at the Charity Hospital of New Orleans, Touro Infirmary, the Hutchinson Memorial, the Richardson Memorial, Hotel Dieu, the Baptist Hospital, Mercy and Presbyterian Hospitals. At the Charity Hospital and Touro Infirmary, the program will be changed in the middle of the week, so that two separate programs will be put on at these two hospitals. The same will apply to the program at the Hutchinson Memorial. Clinics will be given at the Charity Hospital by Dr. George Bel, Dr. J. B. Guthrie, Dr. Amadee Granger, Dr. A. E. Fossier, Dr. J. L. Lewis, Dr. Randolph Lyons, Dr. J. H. Musser, Dr. Robert Bernhard, Dr. W. A. Love, Dr. George R. Herrmann, Dr. Philip Jones, and others. At the Charity Hospital, Dr. Julius Bauer, of Vienna, will give a clinic on certain days.

At the Touro Infirmary, clinics will be given by Dr. L. R. DeBuys and his staff and by Dr. I. I. Lemann and his staff. Dr. DeBuys' staff will limit themselves to diseases of children; Dr. Lemann and his staff to internal medicine and to subjects related to internal medicine more or less closely, so that it is quite possible with the present plan to have a surgeon to discuss cases in which the internist and the surgeon come into close contact, such as thyroid cases, abdominal conditions and so on.

At the Baptist Hospital, Dr. Oscar W. Bethea will run the program.

At Hotel Dieu, Dr. S. Chaille Jamison, Dr. Maurice Couret, Dr. L. A. Fortier and others will give clinics.

At the United States Marine Hospital, Dr. W. C. Rucker will be in charge of the program. There are always a large number of interesting tropical and unusual diseases at the Marine Hospital.

At the Hutchinson Memorial, clinics and demonstrations will be given daily. Dr. Wm. M. James and Dr. J. J. Vallarino, of Panama, will demonstrate their preparations and x-ray findings in amebiasis. Dr. J. C. Small, in addition to his scientific paper, will give in more detail than can be done at a large scientific meeting the particulars of the studies he has made in rheumatic fever. Dr. Robert S. Berghoff will give an afternoon demonstration on the diagnosis of chest diseases; Dr. T. J. Perkins, "Constitutional

Type in Relation to Mental Disease;" Dr. Aldo Castellani, "Fungus Growth;" Dr. C. C. Bass, "Malaria;" Dr. F. M. Johns; Dr. H. W. Butler, "A Slide Method for the Diagnosis of Syphilis;" Dr. Roy H. Turner, "Intestinal Microbiology." A clinical pathological conference will be given one or two days.

The program at the Richardson Memorial will be under the supervision of Dr. J. A. Lanford, who has invited Dr. C. W. Duval, Dr. Henry Laurens, Dr. Irving Hardesty and Dr. J. T. Halsey, Professors of Pathology, Physiology, Anatomy and Pharmacology, respectively, with their staffs, to demonstrate research problems that they are actively engaged in or which they recently completed.

Arrangements are completed for visits to the Leper Colony.

Reduced Fares

Twelfth Annual Clinical Session, New Orleans, La.

The Executive Secretary advises that all railroads of the United States and of eastern Canada have granted reduced fares to our Clinical Session on the Certificate Plan of fare and half fare. Those who attend the Session will purchase going ticket at local railroad office and at the same time request a "Certificate." This Certificate, when validated by the proper officers at the registration booth at New Orleans, will entitle attendant to purchase return ticket a half rate.

These reduced rates apply not only to the attendant, but to dependent members of his family.

Going tickets may be purchased from March 1 to 7, and the return ticket may be used up to March 13. For those who desire to remain in New Orleans longer, the return ticket may be used until March 24, upon deposit of Certificate with W. H. Howard, Special Agent located in the City Ticket Office of the Louisville and Nashville Railroad, New Orleans, upon payment of fee of $1.00 per Certificate receipt at time of deposit.

Special Trains

Twelfth Annual Clinical Session, New Orleans, La.

The Southern Railway System, in conjunction with other railroads of the East, have announced the "Eastern Physicians' Special" train starting from Boston, March 3d, passing through New York, Philadelphia, Baltimore, Washington, to arrive at New Orleans, Monday morning, March 5th. They also announce the "Central States Special," serving eastern Canada and eastern Central States, with connections at Cincinnati and joining the "Eastern Physicians' Special" at Chattanooga and continuing to New Orleans.

Of especial interest is the arrangement for a special train leaving New Orleans after the Convocation on Friday night, March 9th. Heretofore, it often became necessary for many who wished to attend the Convocation to remain over night, because of no suitable train accommodations being available after the Convocation Exercises. This special train has been arranged especially for the convenience of all members who attend the Convocation and wish to leave for the northeastern section of the country immediately thereafter. Time-tables are available in the Executive Secretary's office, and will be distributed to all members residing in the territories served by these special trains.

The route traversed includes the Piedmont Section of Virginia, Blue Ridge Mountain Range, the valleys of the Holston and the Tennessee Rivers, Historical Chattanooga, Industrial Birmingham and across Lake Pontchartrain.

Members residing in the territory served by these trains are requested to make use of them, inasmuch as their comfort and pleasure have been especially arranged for by having them travel together on these trains."

The Executive Offices have on hand a number of old YEAR BOOKS, 1923-24. While these have no present value from the standpoint of directory purposes (the new 1927-28 Year Book was issued during the summer), they may be of interest and his-

torical value to some of our members of more recent election. The Executive Secretary will gladly send a copy to any member upon receipt of 50c in stamps to cover cost of handling and mailing.

NEW ORLEANS

(Contributed by a Resident Fellow of the College)

New Orleans, while more noted for its romantic charm and historic interest, is also a city of modern homes, churches, schools, libraries, beautiful parks and broad, well-paved highways. And it is a city blessed with a climate that makes for perennial out-door activity.

Summer in New Orleans doesn't die in September, shrouded in red autumn leaves. She just kisses the tips of her fingers to the Northland she's been visiting and skips back south again to the Gulf of Mexico where she was born. The Great Lakes can't follow her, nor rock-bound New England, nor the freezing Rockies, but the flowers trip behind her, and the birds go South, and the long steel heartstring of the railroads vibrate with the racing human trainful.

Volumes could be written about New Orleans and the many attractions the visitor will find within her gates. The architectural uniqueness of the building; its shady parks, wood-girded, and reminding one of the haunts of satyrs and nymphs; its inviting driveways, and its unusual historical associations, are features that appeal to all classes of visitors; it has magnificent hotels; its restaurants rank among the finest in the world; it has up-to-date and modern theatres; it has year-round balmy weather, and it has a gracious and hospitable citizenry who delight in entertaining you and hnow how to do so.

Even as New Orleans challenges the world to excel the charm of its French Quarter, so also does it point with proper pride to the picturesqueness of its surroundings as a whole—from the medieval beauty of the "Vieux Carré" to the newer city with its trees and flowers, beautiful homes, monuments, parks, streets, schools and churches.

The bulk of the architectural charm of New Orleans—as well as of its historical and romantic appeal—is found in the "Vieux Carré," or old French Quarter, but by no means all of it. The larger city—the American City, that lies above Canal Street, has its gems of architecture, wonderful and costly mansions facing broad, tree-lined boulevards, beautiful parks and enticing driveways; churches, schools and libraries, magnificent federal, state and civic structures, and those wondrous works of the modern American builder, the skyscrapers that house the great commercial enterprises of today.

The homes of a city are probably the best indication of its prosperity and progressiveness as well as of the culture of its citizenry. Let us then tour over some of the main residential streets of New Orleans.

As we motor out St. Charles Avenue, note the delightful surroundings as well as the architectural beauty of the magnificent homes that border this world famous thoroughfare. There are mansions in St. Charles Avenue that well might rank as palaces, and opening into the street are a number of residence parks, also bordered and centered with palmetto palms—their latticed trunks too big to put your arms around; planted full of spicy camphor trees and long-fronded bananas, spaced out with graceful green fountains of Brazilian date palm.

The houses of the St. Charles district sit back in their gardens, honey-suckled, ivied, covered with jasmine vines, bouqueted by a dozen kinds of roses, with hibiscus torches flaming orange and red before them.

Esplanade Avenue also has its stately homes. It is the avenue of the aristocratic French families and extends from the river to Bayou St. John.

When the Sieur de Bienville, founder of New Orleans, came through Lake Borgne up through the Rigolets and then into the Bayou St. John, in 1718, Esplanade Avenue was an Indian path through a swampy wilderness. How long this trail had been used by the aborigines is not known, but Esplanade Avenue can well be said to be one of the oldest thoroughfares on the continent.

Esplanade Avenue was one of the boun-

daries of the old city as laid out by the Sieur de la Tour, who was Bienville's chief engineer, and became the aristocratic residence street of the latter Creole days. Many of these fine Creole homes, with their spa-spacious grounds, remain.

Below Esplanade Avenue, in what is known as the Third District, is the residential section of small houses. Most of the streets are well paved, affording smooth roads for motoring.

Much of the architectural charm of New Orleans is also found in its old plantation houses. As the cypress swamps on the outskirts of the old city were cleared and turned into plantations, the plantation owners erected beautiful and expensive homes. The usual type is a large, square building surrounded on all four sides with an upstairs and downstairs gallery supported by enormous white columns.

These large plantation houses were built with slave labor out of material that could not be duplicated today at any price. There are also many beautiful ones that are small and compact, with small central portions with small wings balanced on each side. Sometimes there is a gallery on the central portion but not on the wings; and sometimes the galleries are on the wings and not on the central portion.

It has been truly said that "Churches prove the soul of a community"—that they illustrate the sincerity of purpose upon which consciousness is founded; that the city which looks well to its churches need never fear decadence or failure.

New Orleans has many wonderful ancient church structures still used for devotional purposes. New Orleans also has many handsome modern churches representing every denomination.

Christ Church Cathedral, Protestant Episcopal, stands in one of the prettiest portions of St. Charles Avenue at the intersection of Sixth Street.

The First Baptist Church, constructed of stone, is further up the avenue and presents an imposing appearance. A few blocks above is the Rayne Memorial Methodist Church and lower down the Avenue is the costly and stately looking First Methodist Church.

One of the most attractive buildings on St. Charles Avenue is the Touro Synagogue, with its circular bronze roof. Temple Sinai, constructed on the plan of ancient Jewish houses of worship, is in Carondelet Street, further downtown.

Prytania Street Presbyterian Church is a massive structure of stone, in Prytania Street, a block from St. Charles Avenue. Napoleon Avenue Presbyterian Church is another splendid edifice of brick and stone construction. The First Presbyterian Church, which faces Lafayette Square, is one of the oldest of the Protestant churches in the city.

A recent addition to architectural New Orleans is the Mater Dolorosa Catholic Church in Carrollton Avenue. The Catholics have many other fine churches in the city, some of which are: Loyola Church, known as the "Little Jesuit Church," which is on the grounds of Loyola University, facing St. Charles Avenue, opposite Audubon Park; Church of the Immaculate Conception (Jesuits) in Baronne Street; St. Louis Cathedral, one of the most ancient church edifices in America, opposite Jackson Square; Church of the Holy Name, on St. Charles Avenue, and St. Joseph's Church, on Tulane Avenue.

The Christian Scientists have a very beautiful edifice, known as the First Church of Christ Scientist, located on the corner of Nashville Avenue and Garfield Street.

In other articles we have described New Orleans' wonderful museums, the Aquarium, the Art Gallery and other centers of culture. Just a word about its Public Library. The main library building, which was donated by Andrew Carnegie, is located at Lee Circle and St. Charles Avenue. It is of stone and marble construction and the architects copied the design of the Temple of Mars at Rome. The New Orleans library system, which includes the main library and twelve branches, ranks with the finest in the country.

New Orleans is a healthful city. The marked improvement in its health conditions in the past few decades is due in a large

measure to the notable engineering achievements which installed and maintains an unsurpassed system of water supply, sewerage and drainage, upon which there has been expended more than $41,000,000.

New Orleans also has splendid hospitals, including the Charity Hospital, which accommodates the sick of practically all of the city and state and from neighboring states as well.

Charity Hospital was founded in 1832 and has been steadily added to until it now covers four squares. The John Dibert Memorial Tuberculosis Hospital, for which a local philanthropist gave $300,000, is another nationally noted institution.

Among the private hospitals are the Hotel Dieu, Touro Infirmary, Baptist and Presbyterian Hospitals, and Bethany Home.

A unique institution is the Confederate Veterans' Home, out on Bayou St. John. The aged veterans wear uniforms of gray and lead a happy, care-free life.

The mildness of the climate, which permits outdoor life the year-round, makes New Orleans a most healthful place to live in as well as for recreation. Opportunities for hunting and fishing are found within a few miles ride of the city on every side. There is bathing all along the Gulf Coast, in spring, summer and fall, and it is ideal, especially for the kiddies, since there never was and never can be any undertow, thanks to the protecting islands that necklace the shore.

Commercial Exhibit

For some weeks, the Executive Secretary has been promoting and arranging a Commercial Exhibit for the New Orleans Clinical Session. The Exhibit at Cleveland last February was the first large Commercial Exhibit held under the auspices of The College.

Many members expressed gratification with the Exhibit last year. It is not only an interesting feature of the Clinical Session, but is the source of considerable income, which helps to offset the other expenses or conducting a large medical congress. A special effort has been made to lay foundations for this Exhibit which will make it a successful feature in each Clinical Session to come. The securing of exhibitors is not so easily and simply accomplished as some anticipate. Rental booths cost exhibitors from $100 to $150 each. The time of their representatives, the cost of transportation, and the cost of other items render an expense bill usually exceeding $500 in amount. Commercial houses, in business for profit, are unwilling to make these expenditures, unless there is some reasonable return. This "reasonable return" is often measured by the number of attendants visiting the booths.

New Orleans is a city far removed from many of the large manufacturing and publishing centers, and more than ordinary difficulty is likely to be experienced in drawing exhibitors there. The Exhibit Room is in immediate proximity to the registration headquarters, has an unusually attractive location, and contains forty-four booths. At the time this Bulletin goes to press, the following have engaged exhibit booths:

Abbott Laboratories,....North Chicago, Ill.
The Armand Company, Inc.,—
.....Des Moines, Iowa
The Battle Creek Food Co.,—
.....Battle Creek, Mich.
Cameron's Surgical Specialty Co.,—
.....Chicago, Ill.
Deshell Laboratories, Inc.,.....Chicago, Ill.
Charles B. Knox Gelatine Co.,—
.....Johnstown, N. Y.
Lea & Febiger, ...Philadelphia, Pa.
The C. V. Mosby Co., ...St. Louis, Mo.
Sanborn Company, ...Cambridge, Mass.
W. B. Saunders Co., ...Philadelphia, Pa.
Southern Surgical Supply Co.,—
.....New Orleans, La.
Spencer Lens Co., ...Buffalo, N. Y.
Victor X-ray Corporation, ...Chicago, Ill.

Inasmuch as some of these concerns have engaged more than one booth, there are twenty-seven still to be rented. The Executive Secretary seeks the assistance of every member of The College who has any direct contact with commercial exhibitors in disposing of the balance of this space. He has, in his office, charts and complete literature available for distribution.

When the Clinical Session takes place, make it a point, for the good will of The College and your own interest, to visit the exhibits. It will help us to retain the patronage of these companies both for exhibits and for advertising in Annals of Internal Medicine.

Caribbean Cruise

When you are going on a trip, by land or sea, the first thought which flashes across your mind is "Shall I be comfortable?" For within the last decade travel is recognized as a pleasure and not merely as a method of getting from one place to another.

You demand change of scene, hope for

pleasant weather, and insist upon good food, facilities for bathing and dressing, and in addition to these requisites, away down deep in your heart is the thrill of adventure that comes from the desire to see new countries and new people.

What can offer you more than the Caribbean:?

With this in mind a post convention cruise to Havana, Cuba, Panama Canal Zone, and other Caribbean countries is being offered for our members and their families by the United Fruit Company on one of the steamers of its Great White Fleet, the S. S. Cartago.

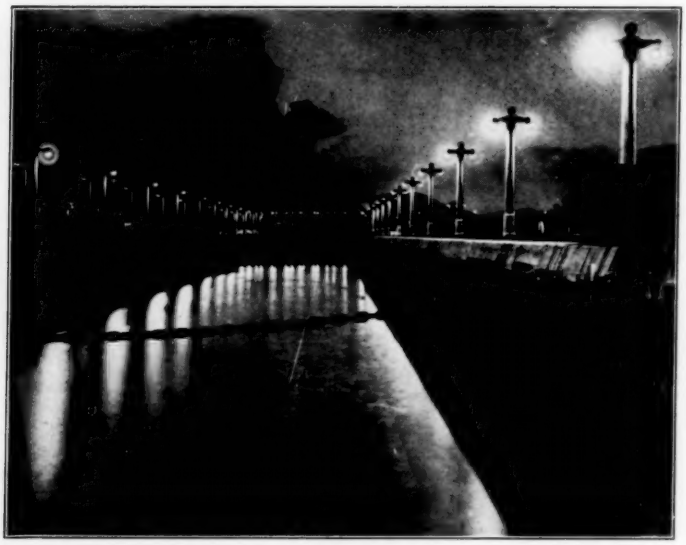
The steamer will sail from New Orleans on March 10th, returning March 26th and during that time will visit lands of perpetual summer. Not the scorching heat of our more Northern latitudes in July and August; rather the calm delightful atmosphere of a June afternoon. A land where Westerly Trade winds bring health and healing in their train, where the sapphire sea ripples over coral roofs in lazy content and where, after gorgeous sunsets, the stars gleam like golden lamps in an indigo sky.

Ponce de Leon sought for a Spring of Perpetual Youth unaware that all around him was the rejuvenating sea and air and sky which in the passing years have brought renewed health and spirits to the thousands who have experienced the charm of the Caribbean.

For the Caribbean leaves more than a passing impression. It has the undefineable charm of good music, wonderful architecture, of beautiful women; and every year visitors from all parts of the world return knowing that they will find something new, something delightful to

enchant their senses and bring them back again.

Imagine, if you please, a Great White Fleet Ship with spacious decks, flooded with sunshine, and shaded with awnings, beneath which are companionable deck chairs. White clad stewards are passing tea, bouillon and things good to eat. Here and there are groups of the more athletic engaged in deck billiards, shuffle-board and in the card room other groups are busily engaged. At night colored electric lights illuminate the decks; and orchestra plays softly and dancing is going on for we are in the Gulf Stream, steaming steadily south and the ship moves so steadily that motion is sensed rather than felt.



Two days of this luxurious travel, and we are at Havana, "Paris of America". You'll find here a quaint commingling of old and new which has to be felt and seen rather than read about. Spain built mighty fortresses in Havana. Today they lie idle in the tropic sun. The first mass ever celebrated in the Western Hemisphere was at El Templete, and a stately cathedral still takes one's mind back to the day when soldier and priest worked together. Today the tourist seeks the wonderful shops in O'Reilly street, listens to the band on the Prado or hurries out to the race track where during the season the Sport of Kings is at its best. Special automobile trips are made to all the places of interest in Havana and the traveler is indeed blasé who cannot find every day something new and interesting to enchain his attention.

We are on an imaginary cruise remember, so suppose we next steam south across the Caribbean furrowing the same path over which sailed Columbus, Drake, Frobisher, Anson and the long list of pirates which later swarmed in the "Spanish Main." A faint blue line on the horizon and we raise Cristobal, the modern American town which guards the Atlantic entrance to the Panama Canal. An inspection of the Canal is an education. The massive locks, the

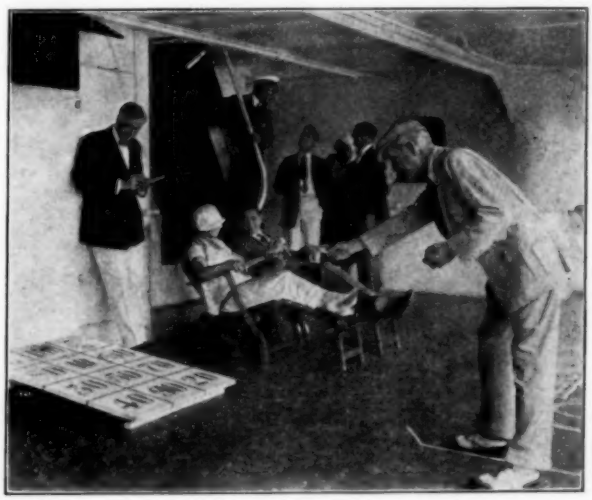
scarp of the great dam at Gatun, the mechanical perfection of the methods by which ocean liners and great battleships are raised and lowered in the "pathway of the East and West," is a complete and wonderful illustration of American Engineering.

We sail through the man-made waterway on a reconditioned torpedo boat destroyer and note how the genius of Americans tore asunder the barrier between the Atlantic and the Pacific and we are proud that we belong to the Great Republic of the West that made all this possible. Of the Historic interest we shall say little. But it was at old Panama that Sir Henry Morgan, greatest of all pirates sacked and burned the stronghold of Old Spain and the ruins of the violated cathedral stand there today.

And during all these days of sightseeing you must remember that the Great White ship is your home. So thoroughly do you feel the meaning of the word "home" that you always appreciate your return to its shaded decks and the ministrations of stewardesses, waiters and deck attendants. The days pass on golden wings. Your wants are understood and gratified almost before you can give them utterance. Your room is spacious and airy. Your bath is a thing of delight for here you will find hot and cold water, salt and fresh. Special trips are planned in advance. In fact if you are a bit jaded from business or social cares, if you feel the need for luxurious comfort, good food, special attention and a complete change of air, scenery and environment you will find a Cruise to the Caribbean a panacea for nearly all the cares and troubles human flesh is heir to.

In addition to affording opportunity for an enjoyable cruise to foreign lands with our own members as fellow passengers, advice has been received that if the party desires, clinics on clinical medicine will be arranged at the United States Government Hospital at Ancon, Canal Zone, Santo Tomas Hospital and the Herrick Clinic, Panama. Furthermore, Dr. W. E. Deeks, General Manager, Medical Department of the United Fruit Company, has also kindly offered to arrange a clinic at their hospital in Castilla, Honduras—one of the several hospitals operated by that Company in the tropics.

The party will be strictly limited to seventy-five passengers and as the demand is expected to greatly exceed this number, those desiring to go are urged to consummate ar-



rangements as early as possible. Reservation requests should be accompanied by a deposit of fifty dollars ($50.00) per person, balance to be paid not later than February 25th. Reservations should be secured directly through one of the following officials of the United Fruit Company:

H. C. Hicks, A. P. T. H., United Fruit Company, 321 St. Charles Ct., New Orleans, La. L. P. Jones, G. W. P. A., United Fruit Company, 203 S. Dearborn St., Chicago, Ill.

Further information and literature will gladly be supplied upon request to the officers mentioned, or inquiries may be sent through the Executive Secretary's office in Philadelphia.